Network Systems Science & Advanced Computing

Biocomplexity Institute & Initiative

University of Virginia

Estimation of COVID-19 Impact in Virginia

December 22nd, 2021

(data current to December 10th – 14th)

Biocomplexity Institute Technical report: TR 2021-129

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About Us

- Biocomplexity Institute at the University of Virginia
  - Using big data and simulations to understand massively interactive systems and solve societal problems
- Over 20 years of crafting and analyzing infectious disease models
  - Pandemic response for Influenza, Ebola, Zika, and others

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Overview

- **Goal**: Understand impact of COVID-19 mitigations in Virginia
- **Approach:**
  - Calibrate explanatory mechanistic model to observed cases
  - Project based on scenarios for next 4 months
  - Consider a range of possible mitigation effects in "what-if" scenarios
- **Outcomes:**
  - Ill, Confirmed, Hospitalized, ICU, Ventilated, Death
  - Geographic spread over time, case counts, healthcare burdens

Key Takeaways

Projecting future cases precisely is impossible and unnecessary.
Even without perfect projections, we can confidently draw conclusions:

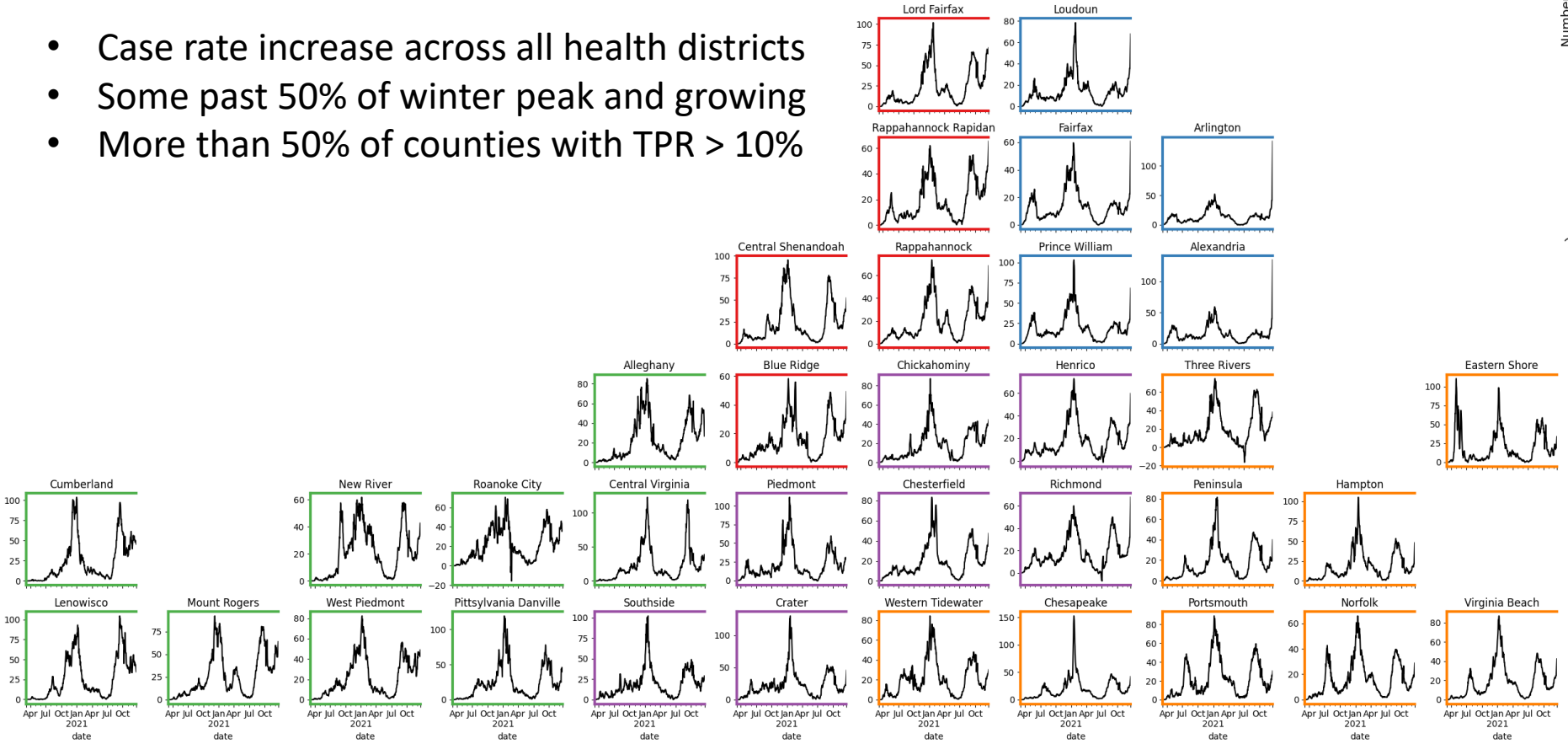
- **Case rates grew after holiday break but growth has slowed slightly, keeping case rates high as the anticipated arrival of Omicron may fuel more rapid growth in the near term**
- VA 7-day mean daily case rate up to 38.5/100K from 30/100K; US is up to 44/100K (from 36/100K)
- Projections show a continued rise of cases which becomes more extreme under Omicron and FallWinter scenarios that anticipate likely drivers of future transmission
- Recent updates:
  - Overhauled model structure further refined to better capture different tiers of immunity and the immune evasion of the Omicron variant
  - Analysis of the effects of increasing 3rd dose coverage

The situation continues to change. Models continue to be updated regularly.

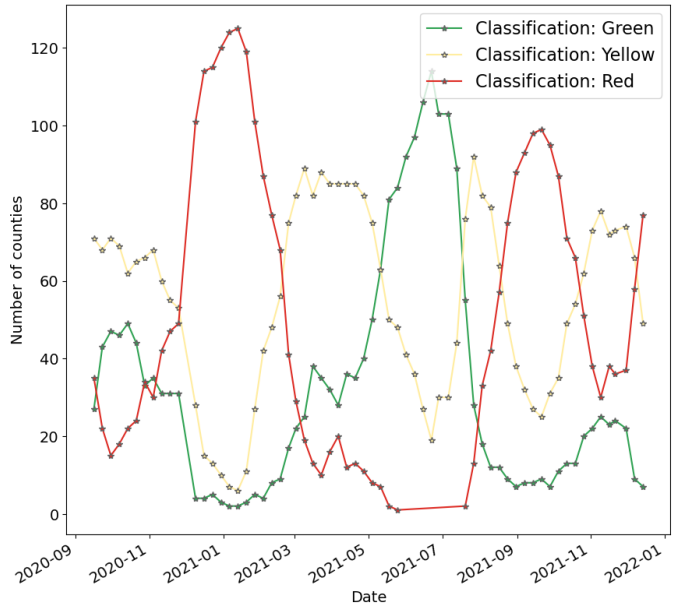
Situation Assessment

Case Rates (per 100k) and Test Positivity

- Case rate increase across all health districts
- Some past 50% of winter peak and growing
- More than 50% of counties with TPR > 10%



Data source: https://data.cms.gov/covid-19/covid-19-nursing-home-data



County level RT-PCR test positivity

Green: <5.0% (or <20 tests in past 14 days)

Yellow: 5.0%-10.0% (or <500 tests and <2000 tests/100k and >10% positivity over 14 days)

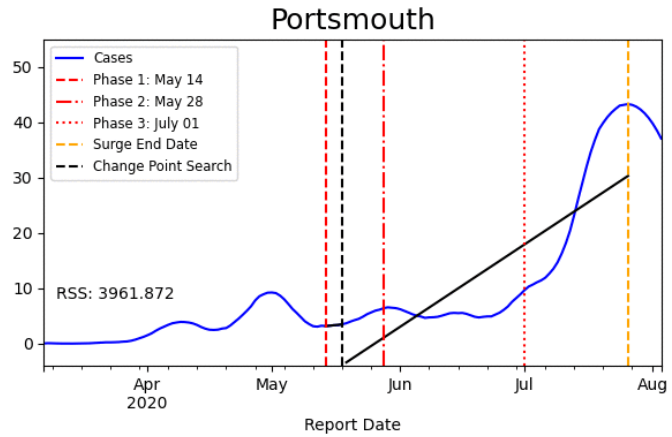
Red: >10.0% (and not "Green" or "Yellow")

District Trajectories

Goal: Define epochs of a Health District's COVID-19 incidence to characterize the current trajectory

Method: Find recent peak and use hockey stick fit to find inflection point afterwards, then use this period's slope to define the trajectory

Hockey stick fit

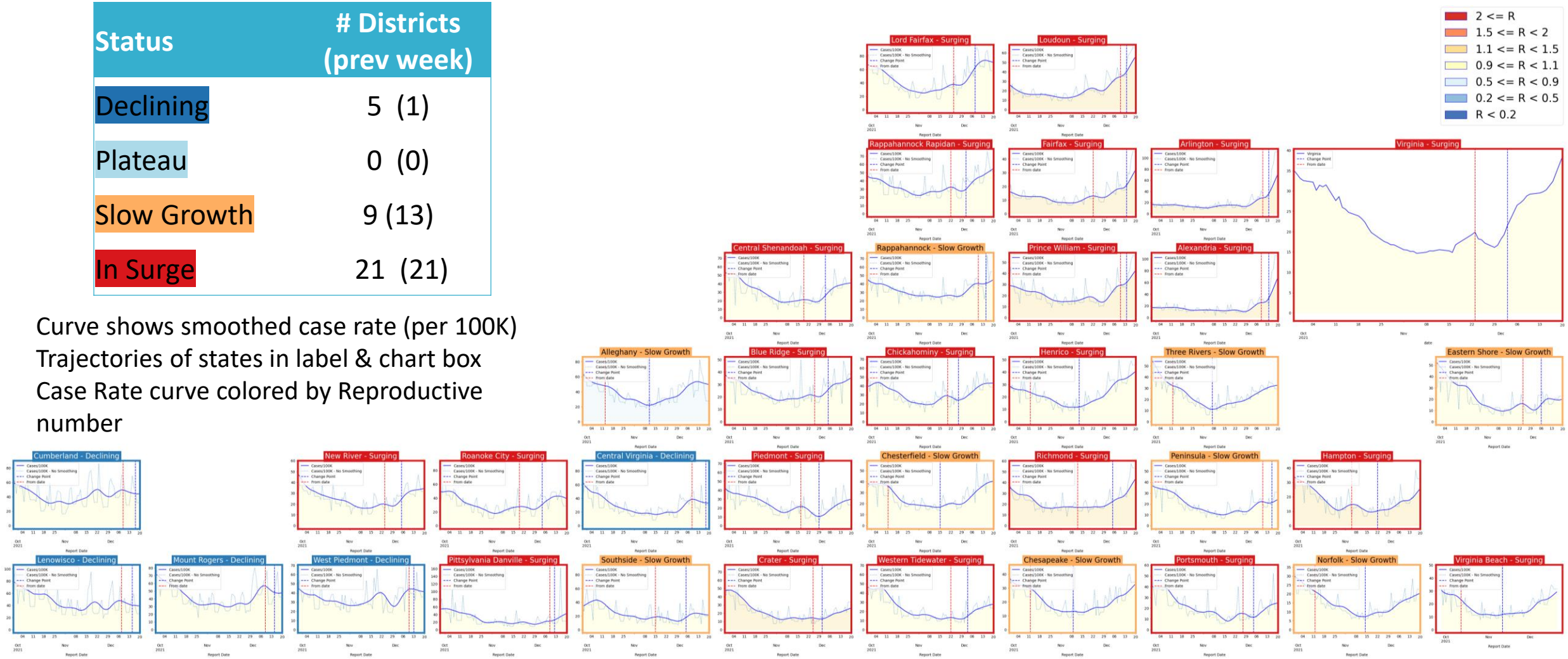


Trajectory	Description	Weekly Case Rate (per 100K) bounds	# Districts (prev week)
Declining	Sustained decreases following a recent peak	below -0.9	5 (1)
Plateau	Steady level with minimal trend up or down	above -0.9 and below 0.5	0 (0)
Slow Growth	Sustained growth not rapid enough to be considered a Surge	above 0.5 and below 2.5	9 (13)
In Surge	Currently experiencing sustained rapid and significant growth	2.5 or greater	21 (21)

District Trajectories – last 10 weeks

Status	# Districts (prev week)
Declining	5 (1)
Plateau	0 (0)
Slow Growth	9 (13)
In Surge	21 (21)

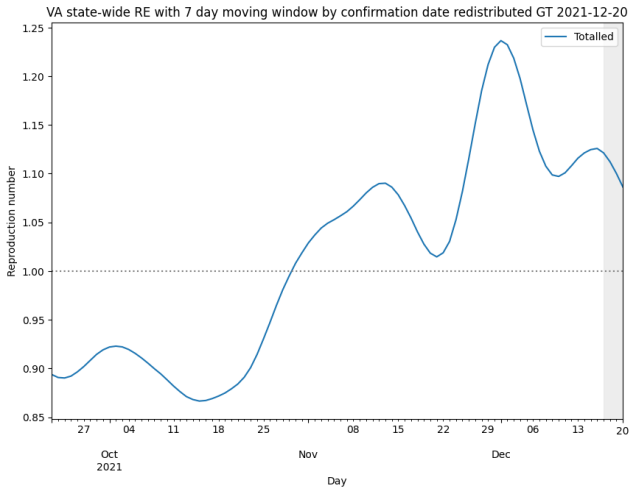
Curve shows smoothed case rate (per 100K)
Trajectories of states in label & chart box
Case Rate curve colored by Reproductive number

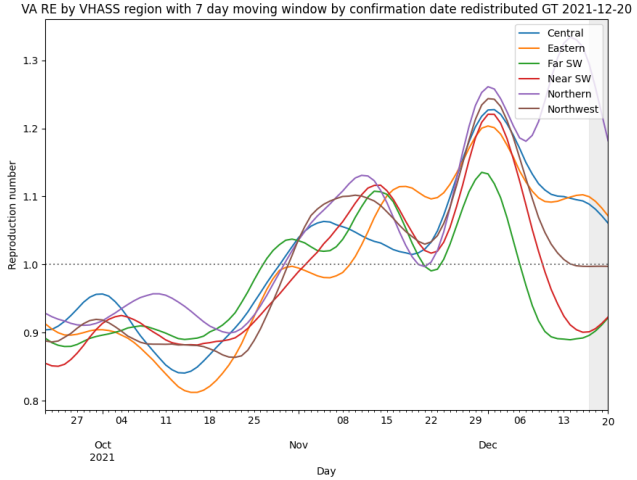


Estimating Daily Reproductive Number – Redistributed gap

Dec 20th Estimates

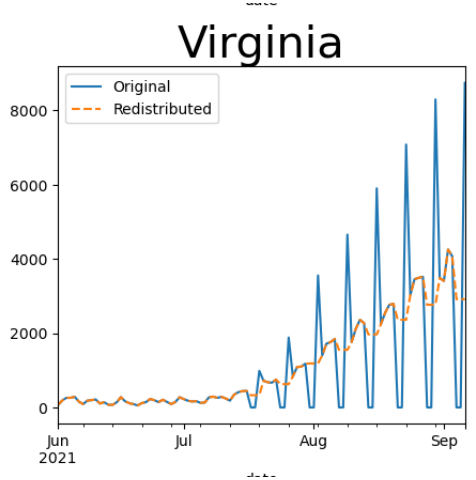
Region	Date Confirmed R_e	Date Confirmed Diff Last Week
State-wide	1.116	-0.002
Central	1.059	0.002
Eastern	1.072	0.051
Far SW	0.919	0.025
Near SW	0.923	-0.086
Northern	1.181	0.149
Northwest	0.996	-0.056





Skipping Weekend Reports & holidays biases estimates

Redistributed "big" report day to fill in gaps, and then estimate R from "smoothed" time series



Methodology

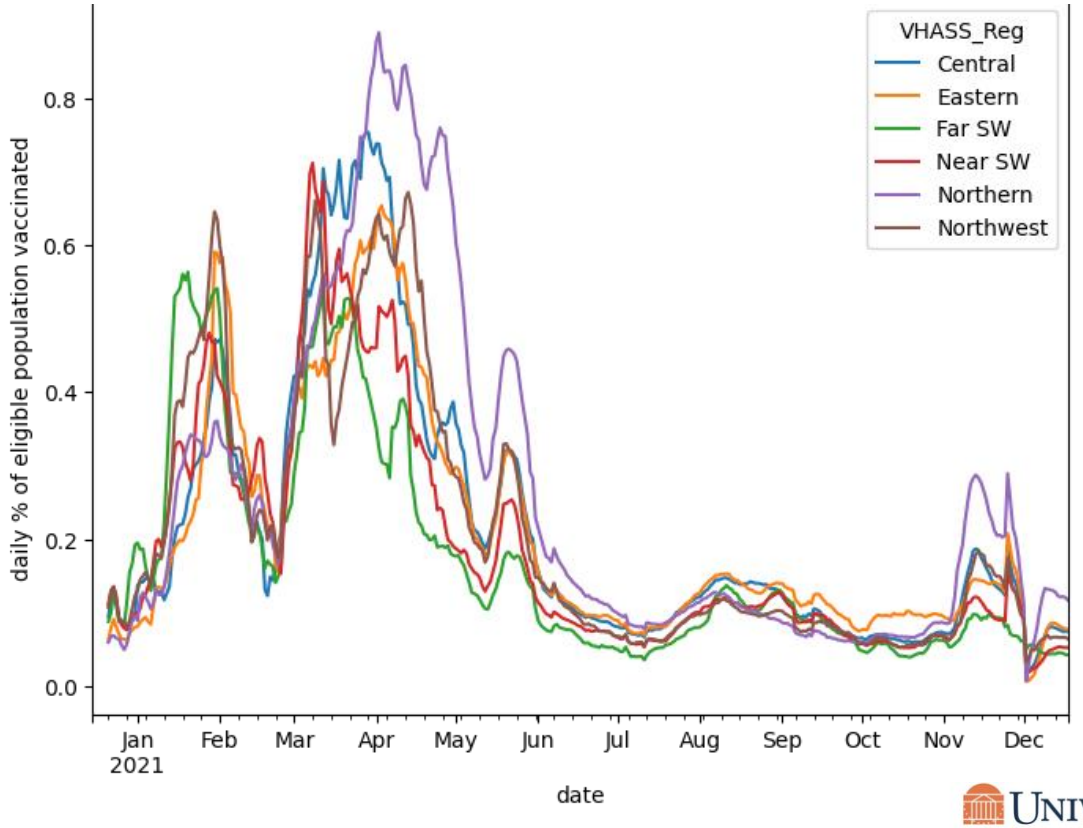
- Wallinga-Teunis method (EpiEstim[1]) for cases by **confirmation date**
- Serial interval: updated to discrete distribution from observations (mean=4.3, Flaxman et al, Nature 2020)
- Using Confirmation date since due to increasingly unstable estimates from onset date due to backfill

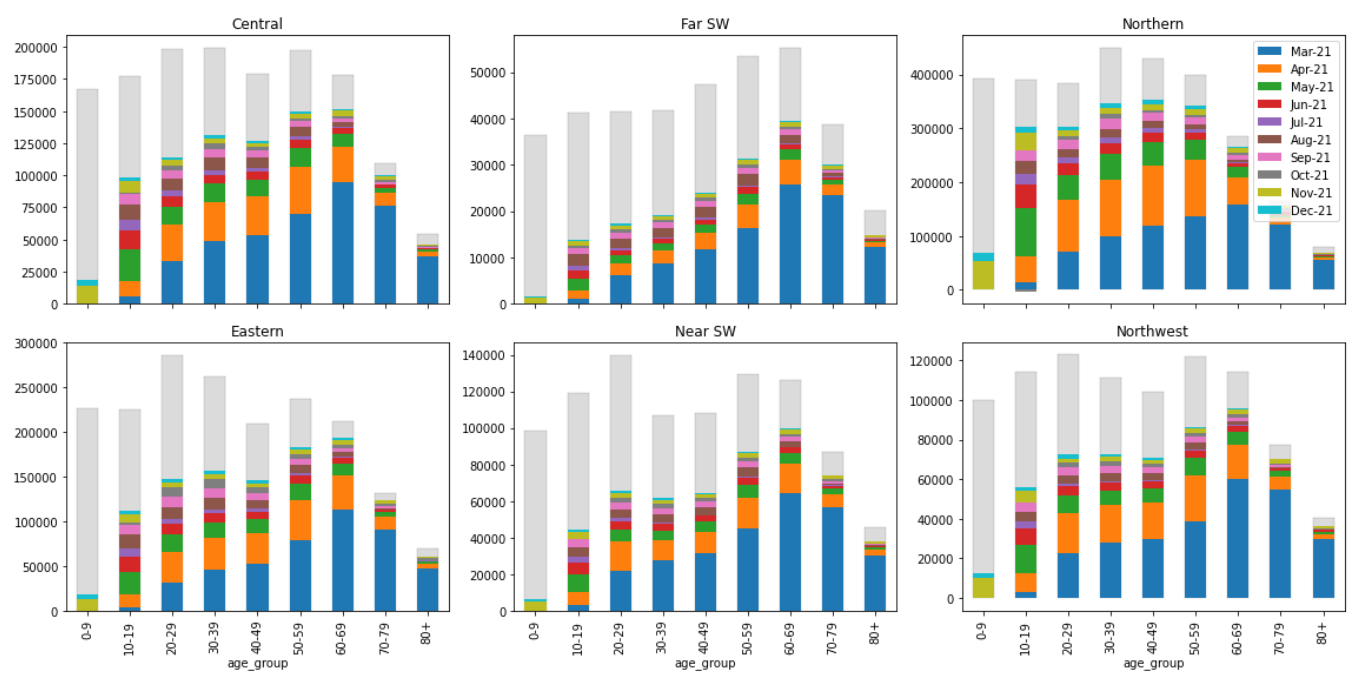
1. Anne Cori, Neil M. Ferguson, Christophe Fraser, Simon Cauchemez. A New Framework and Software to Estimate Time-Varying Reproduction Numbers During Epidemics. American Journal of Epidemiology, Volume 178, Issue 9, 1 November 2013, Pages 1505–1512, https://doi.org/10.1093/aje/kwt133

Vaccination Administration Slow

Regional Vaccine courses initiated per day (% eligible):

- Proportion eligible for first dose of vaccines across regions (in the ~0.1% or 100 per 100K a day)
- Age-specific proportions of population vaccinated show recent progress in younger ages



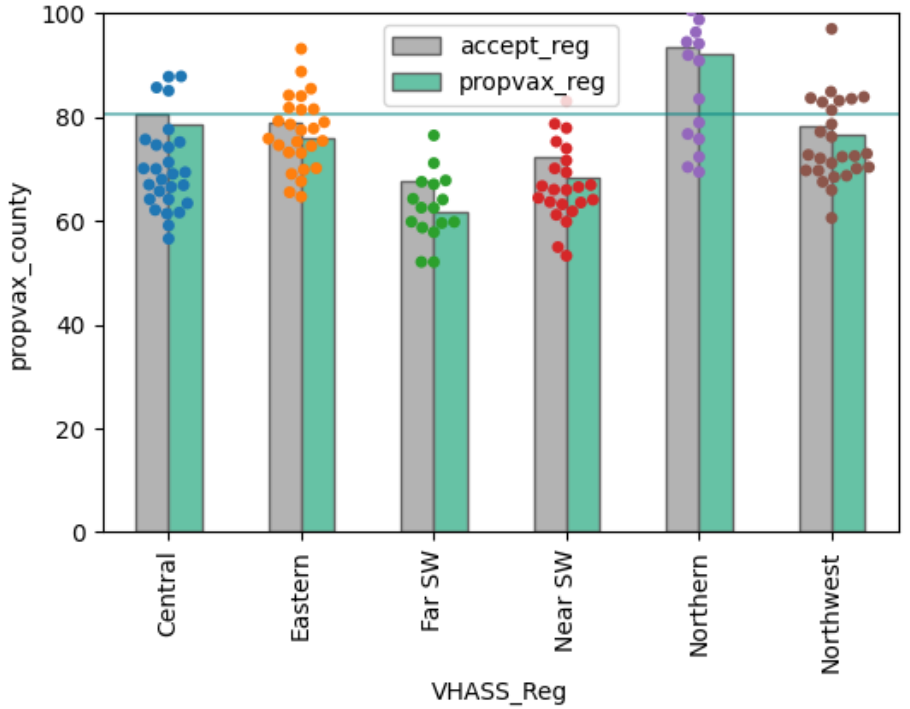


Vaccination Acceptance by Region

Corrections to surveys:

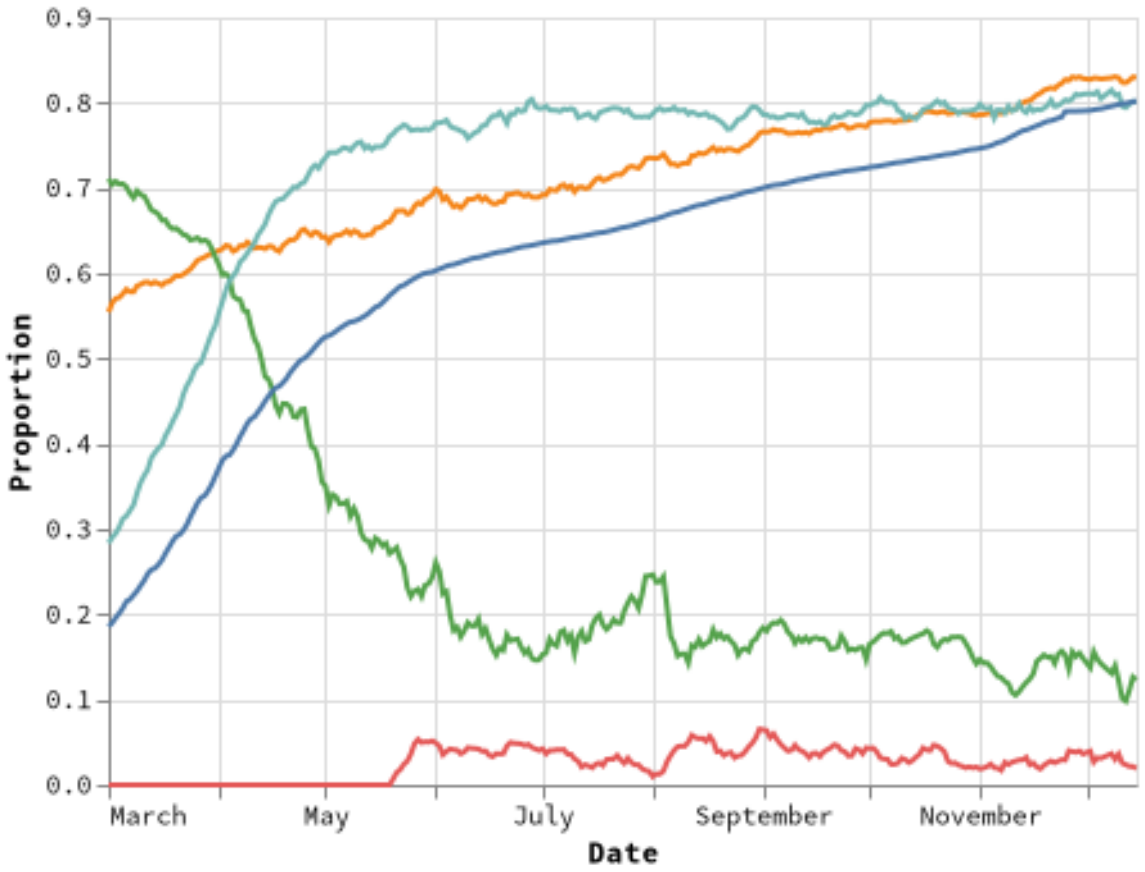
- Facebook administered survey is timely and broad, but biased by who accesses Facebook and answers the survey
- Correction approach:
  - Calculate an over-reporting fraction based on reported vaccinations compared to VDH administration data
  - Cross-validate coarse corrections against HPS survey at the state level and corrected in same manner

Region	COVIDcast accepting corrected	VDH proportion pop vaccinated
Central	80%	78%
Eastern	79%	75%
Far SW	65%	62%
Near SW	72%	68%
Northern	94%	92%
Northwest	78%	76%
Virginia	**83%**	**80%**



Grey Bar: Survey measured and corrected acceptance
Green Bar: Proportion of eligible population administered a vaccine
Dots: Proportion administered at least one dose for each county

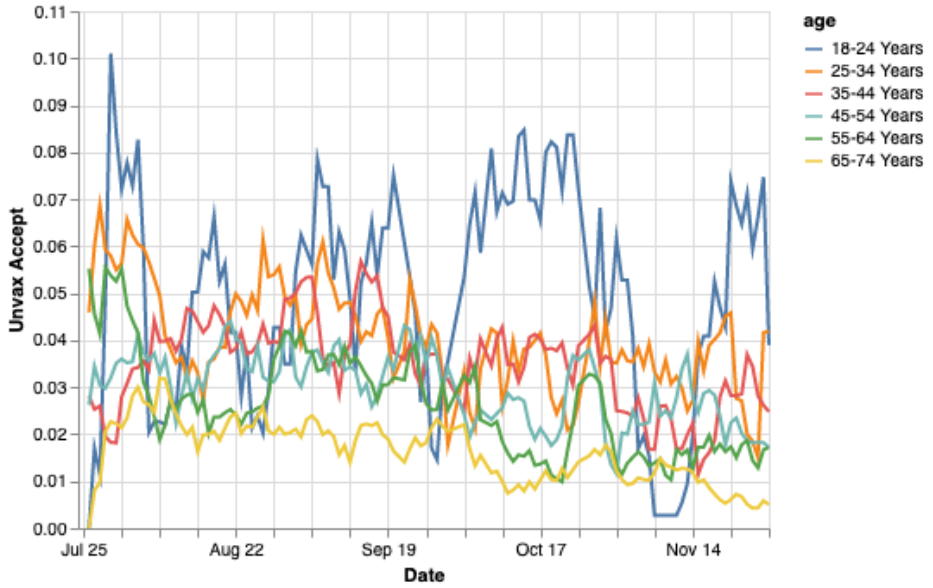
Vaccine Acceptance Components over Time



Vaccine Acceptance adjusted to include scheduled appointments

- Steady rise in acceptance over the past couple months
- Unvaccinated Acceptance shows ~20% of those who are unvaccinated are definitely or probably willing to be vaccinated
- Scheduled appointments for vaccination have increased through August but seem to be leveling off

Acceptance Across Age groups among Unvaccinated

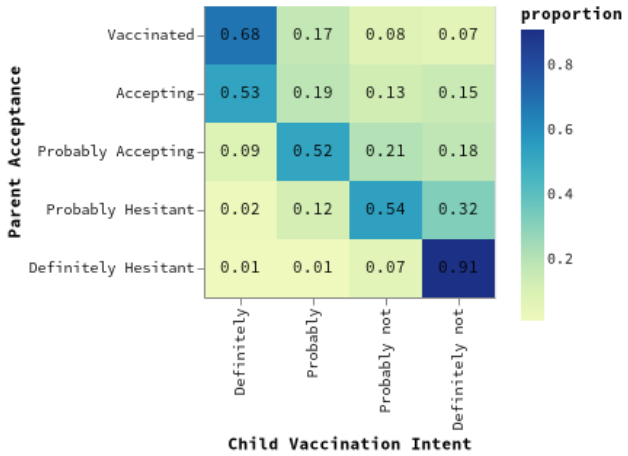


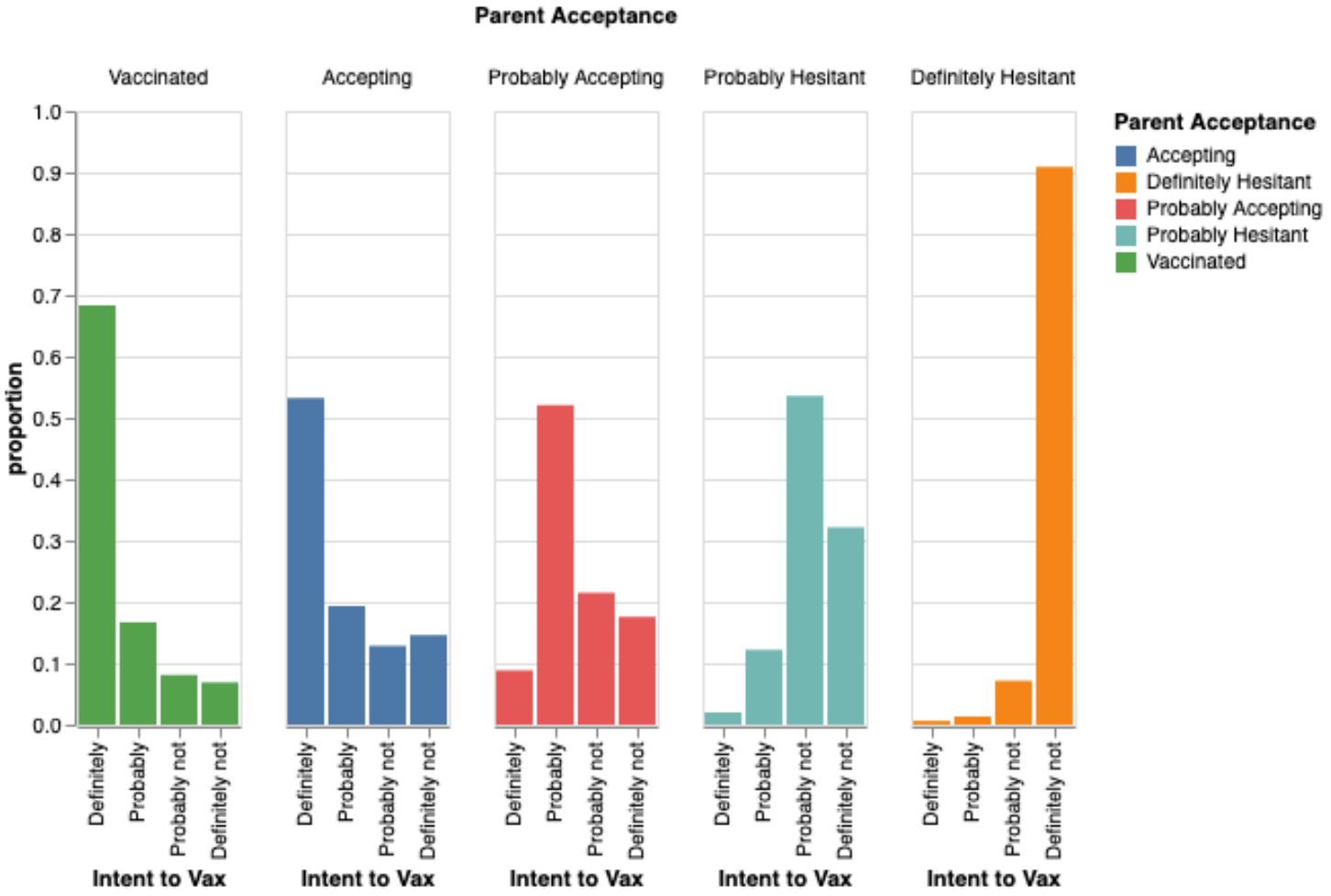
Data Source: https://covidcast.cmu.edu

Parental Intention to Vaccinate Children

Parental Intention to Vaccinate Children lower than overall Acceptance

- Most willing (vaccinated) remain at ~70% definitely intending to vaccinate kids
- Intention strongly biased by the willingness of the parent, and skews towards unwillingness to vaccinate





Data Source: https://covidcast.cmu.edu

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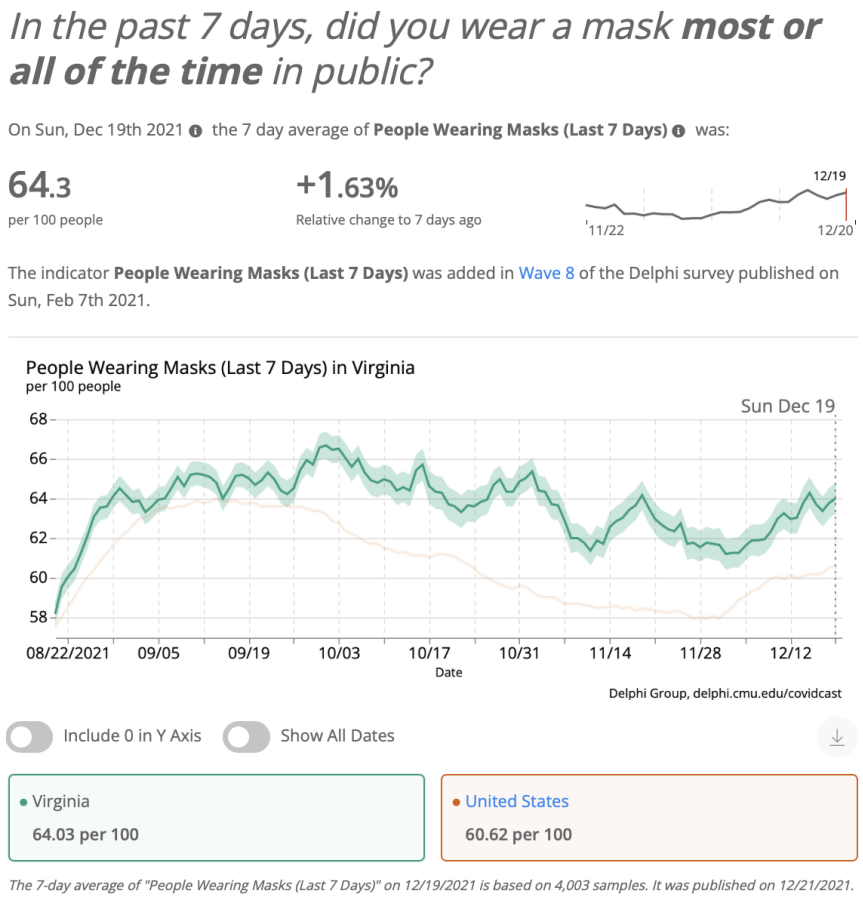
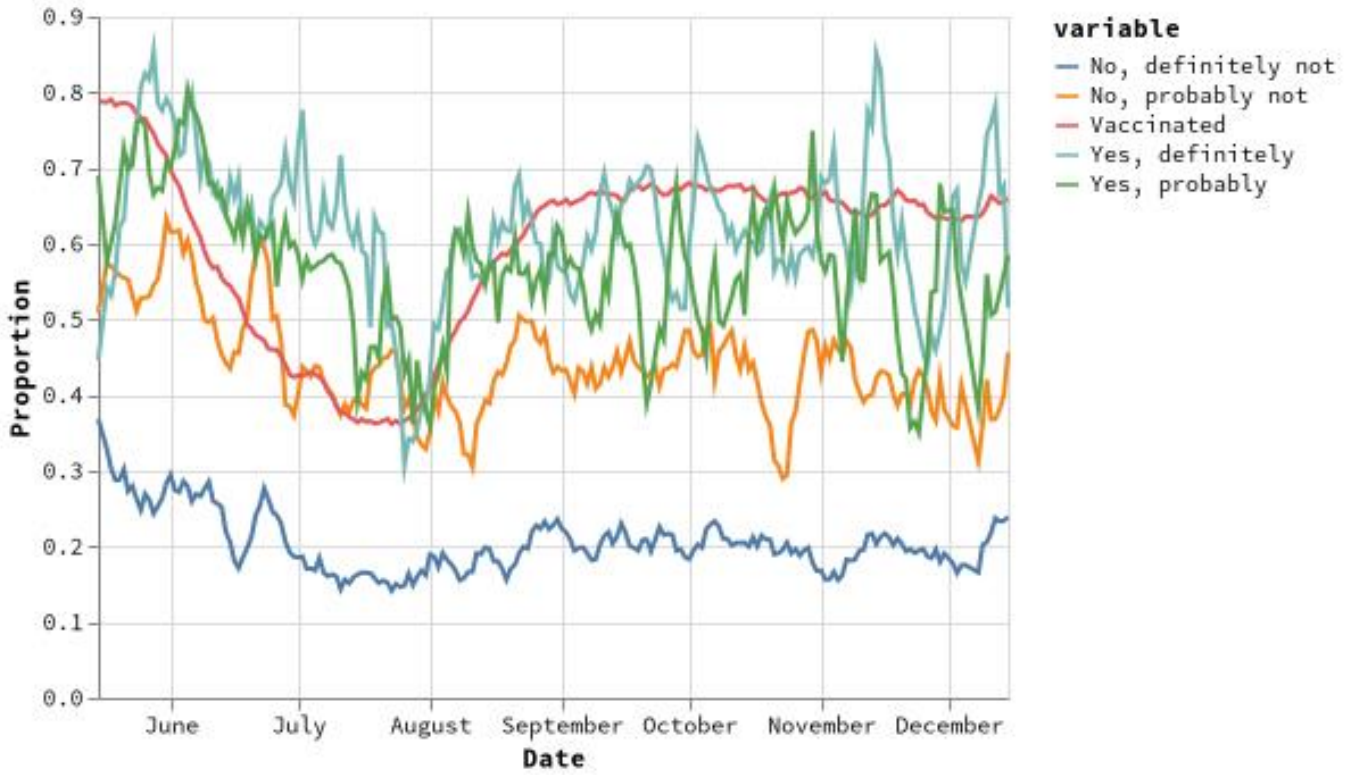
Mask Usage Stalls

Self-reported mask usage has increased slightly to ~64% (mid 60s in previous months)

- US and VA experienced similar small ticks up
- Mask wearing remains lower amongst unvaccinated especially among least willing to be vaccinated



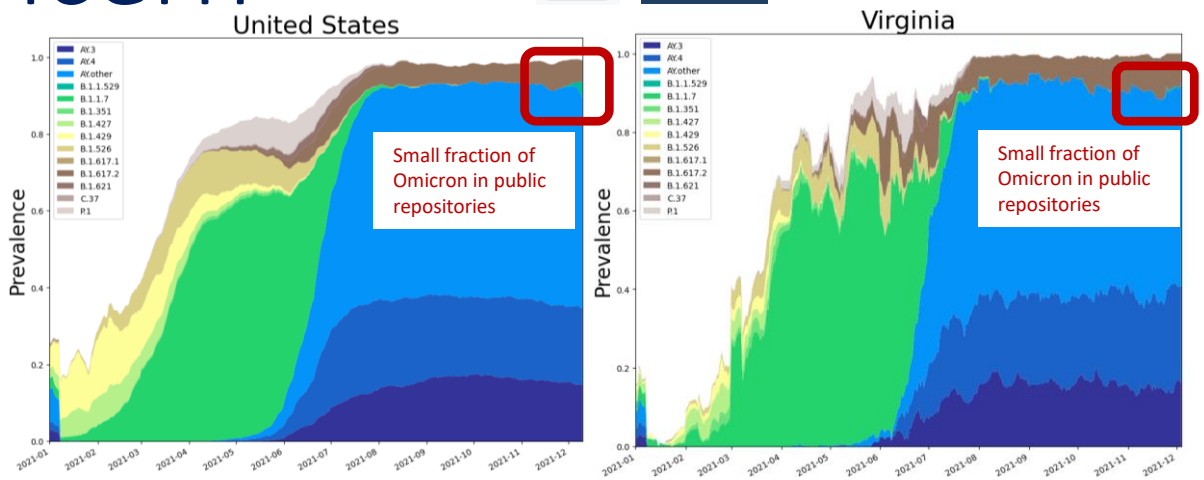


Data Source: https://covidcast.cmu.edu

SARS-CoV2 Variants of Concern

Emerging new variants will alter the future trajectories of pandemic and have implications for future control

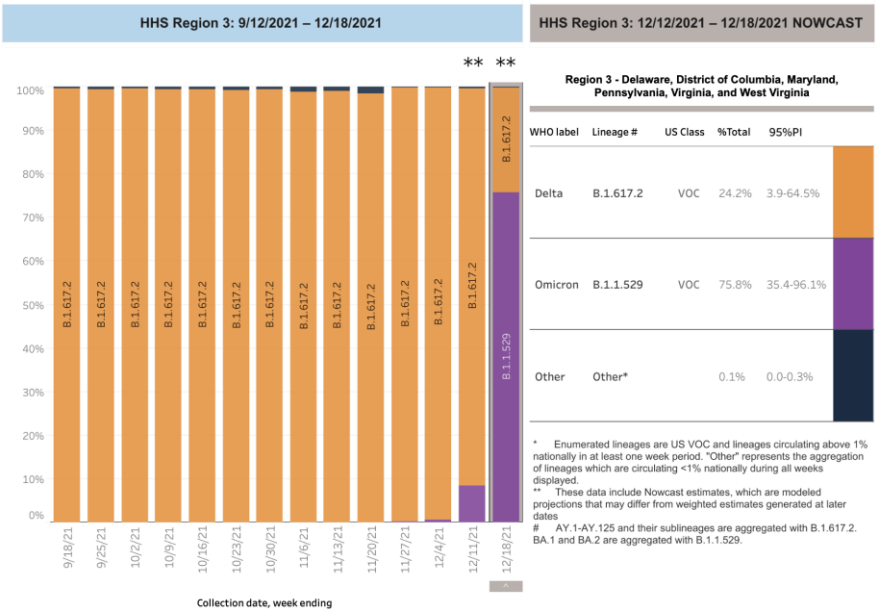
- Emerging variants can:
  - Increase transmissibility
  - Increase severity (more hospitalizations and/or deaths)
  - Limit immunity provided by prior infection and vaccinations
- Genomic surveillance remains very limited
  - Challenges ability to estimate impact in US to date and estimation of arrival and potential impact in future



WHO label	Pango lineage*	GISAID clade	Nextstrain clade	Additional amino acid changes monitored*	Earliest documented samples	Date of designation
Alpha	B.1.1.7	GRY	20I (V1)	+S:484K +S:452R	United Kingdom, Sep-2020	18-Dec-2020
Beta	B.1.351	GH/501Y.V2	20H (V2)	+S:L18F	South Africa, May-2020	18-Dec-2020
Gamma	P.1	GR/501Y.V3	20J (V3)	+S:681H	Brazil, Nov-2020	11-Jan-2021
Delta	B.1.617.2	G/478K.V1	21A, 21I, 21J	+S:417N +S:484K	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021
Omicron*	B.1.1.529	GRA	21K, 21L	+R346K	Multiple countries, Nov-2021	VUM: 24-Nov-2021 VOC: 26-Nov-2021

World Health Organization [WHO](#)

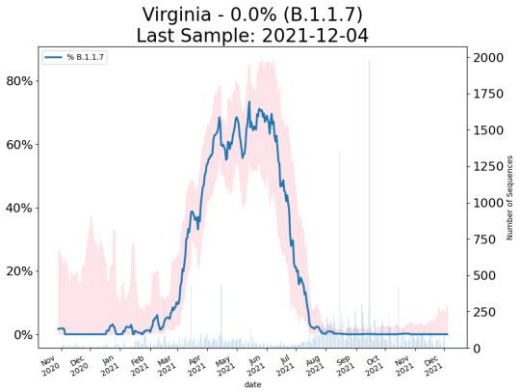
Omicron Prevalence
SIGNIFICANTLY revised from last week
Region 3:
8.4% to 76% in a week
~3 doublings
National:
12% to 73% in a week
~ 3 doublings



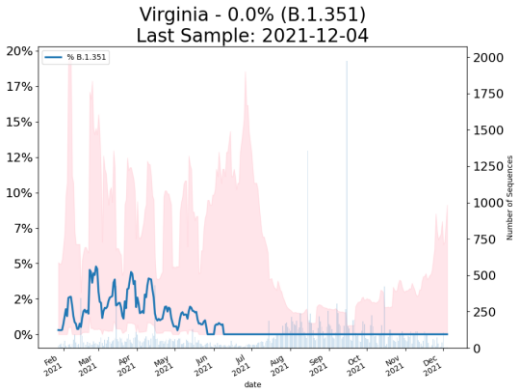
CDC [CDC Variant Tracking](#)

SARS-CoV2 Variants of Concern

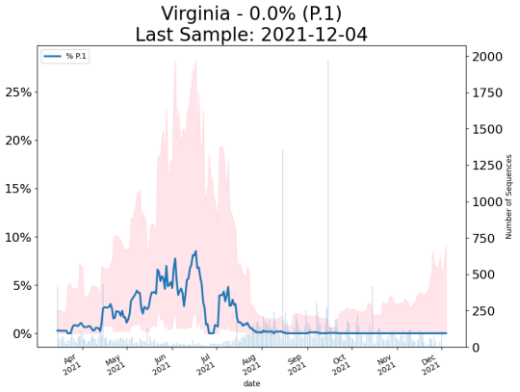
Alpha α - Lineage B.1.1.7



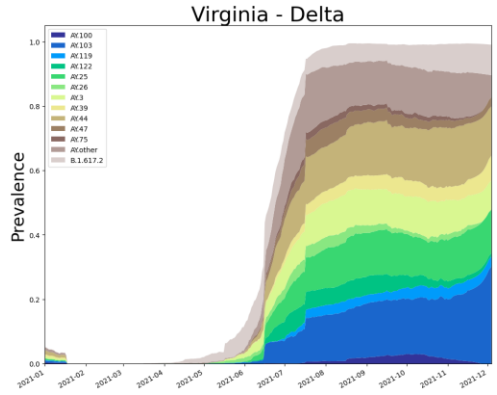
Beta β - Lineage B.1.351



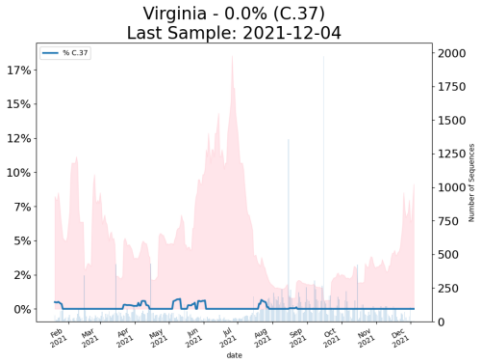
Gamma γ - Lineage P.1



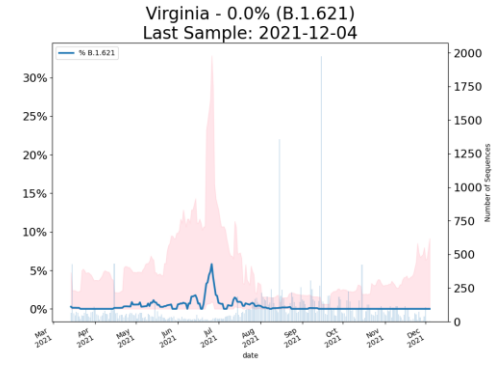
Delta δ - Lineage B.1.617.2



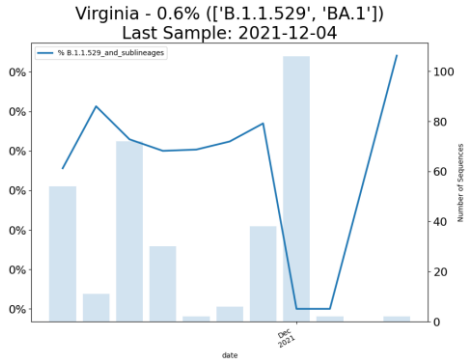
Lambda λ - Lineage C.37

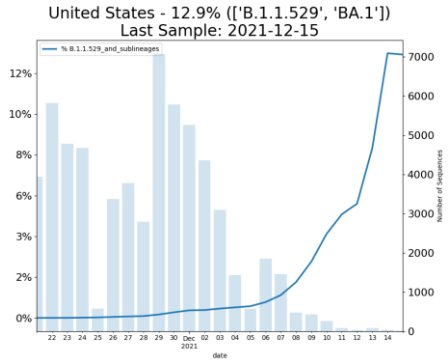


Mu μ - Lineage B.1.621



Omicron ο - Lineage B.1.1.529



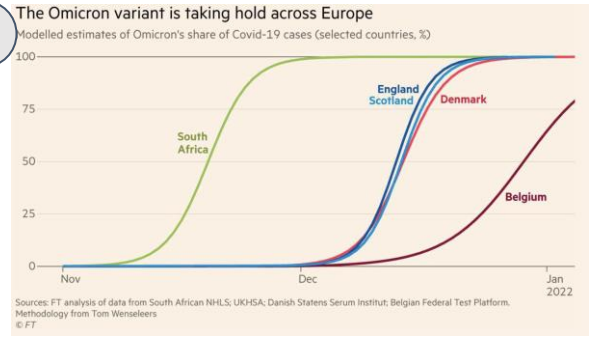


Omicron – Prevalence and Growth

Omicron has become dominant fast and fuels case rate growth

1. Experience of South Africa is being followed in several European nations (Financial Times)
2. Omicron now dominant strain in UK (below 1% to 50% in 2 weeks), growth of SGTF% in UK remains exponential, with only slight slowing (Twitter)
3. ECDC modeling estimates predominance in early 2022 for Europe (ECDC via Twitter)
4. Univ Washington and Yale both report over 10% for recent SGTF%
5. Case Rate growth in countries with lots of Omicron has been more rapid than previous waves (Our World in Data)

1



https://www.ft.com/content/3c27c135-fdbc-4db7-8c7c-6e1f6c386235

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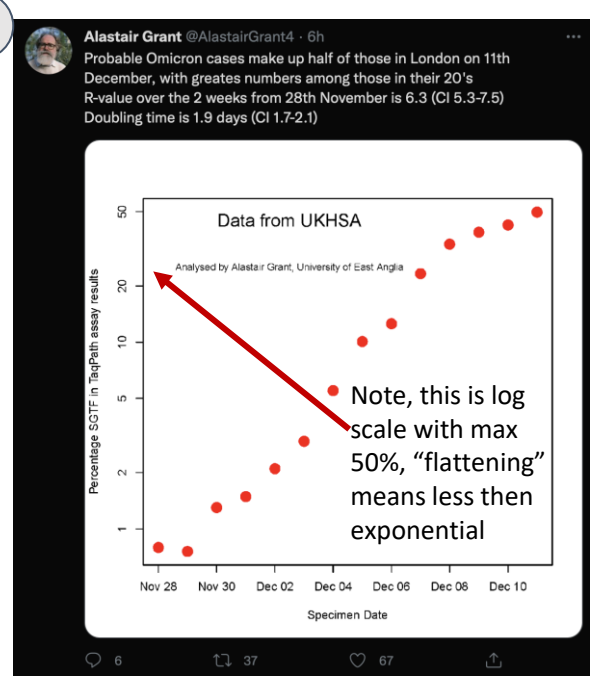

https://twitter.com/AlastairGrant4/status/1471032314436235268

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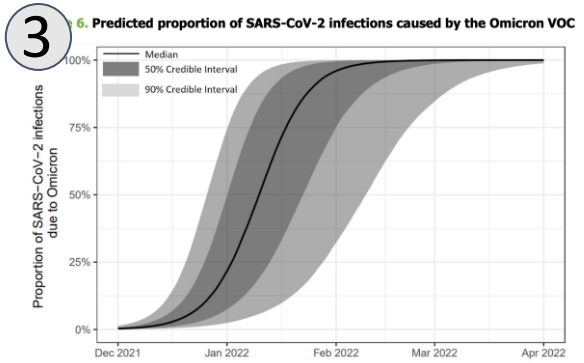

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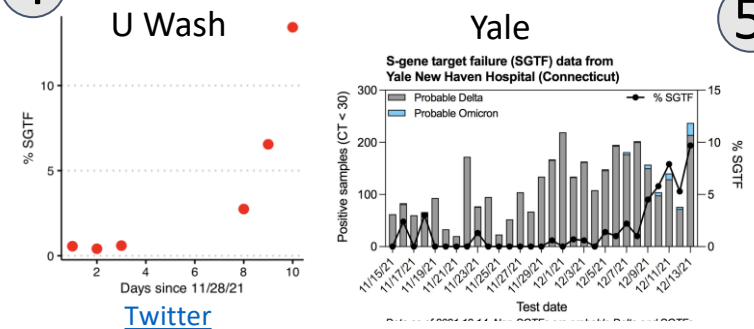

Twitter

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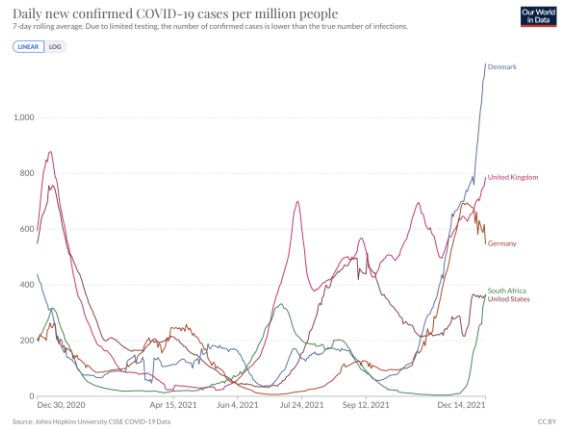

Our World in Data

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Omicron – Immune Evasion and Transmissibility

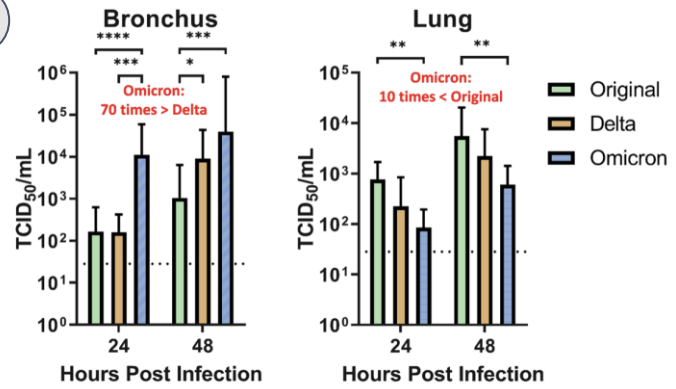
Lab Studies find Omicron to be more transmissible and immune evading

1. Study from Hong Kong shows Omicron to be much more efficient at infecting Bronchus cells, though slightly less in Lung cells (HKU)

2. In vitro study finds antibody neutralization of Omicron to be much stronger from serum from individuals with a 3rd dose of mRNA vaccine than just 2 doses (non-peer reviewed preprint)

3. Initial analysis of Omicron mutations suggest there is minimal evasion against T-cell mediated immune response, thus T-cell mediated immunity should remain robust against Omicron, ie infection may occur but immune response will still occur (BioArxiv)

1



University of Hong Kong

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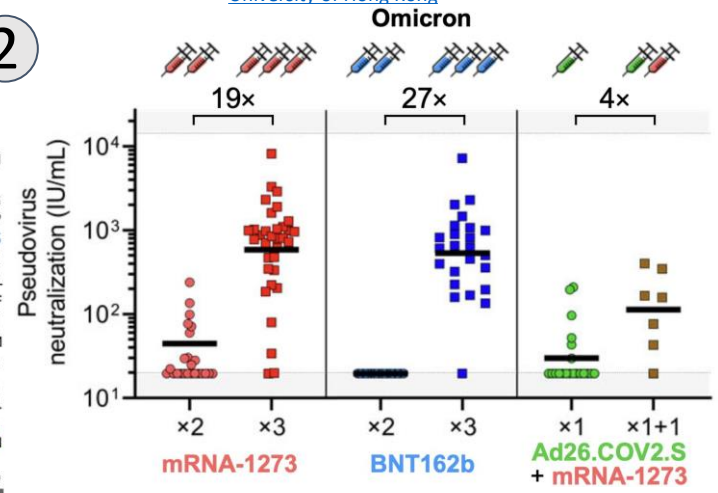
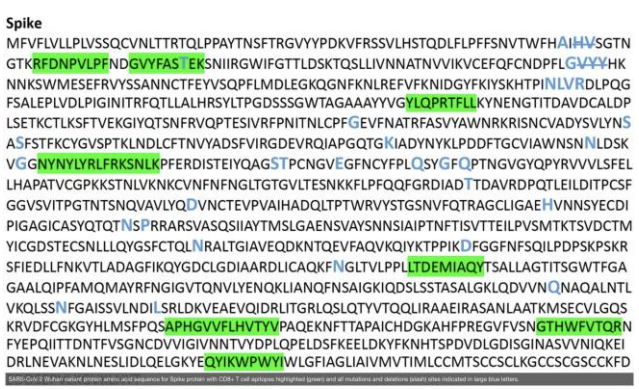


Balzas Lab Preprint

3



BioArxiv

Omicron – Severity

S+ = Not Omicron
S- = Proxy for Omicron

Assessing the severity of Omicron is challenging due to different risks by age, levels of immunity, types of vaccines used across the different populations affected by Omicron to date

1. Study from Imperial College's MRC found no evidence that Omicron cases were less likely to be admitted to hospital (and were much more likely to cause re-infection)
2. Recent study from South Africa found an adjusted OR of 0.3 for severe disease for Omicron compared to Delta, (severe disease defined as requiring ICU or similar advanced care)

1

Class	Variable	S+	S-	log(OR)	OR	p-value
Time	Day	208947	15087	0.43 (0.42-0.44)	1.54 (1.53-1.55)	<1e-6
NHS Region	London	21585	5976	0	1	-
	East of England	27986	2274	-0.85 (-0.91--0.79)	0.43 (0.4-0.46)	<1e-6
	Midlands	41223	1645	-1.53 (-1.59--1.46)	0.22 (0.2-0.23)	<1e-6
	North East and Yorkshire	45631	811	-2.32 (-2.41--2.24)	0.1 (0.09-0.11)	<1e-6
	North West	34726	1998	-1.11 (-1.17--1.04)	0.33 (0.31-0.35)	<1e-6
	South East	27405	1985	-0.85 (-0.92--0.79)	0.43 (0.4-0.45)	<1e-6
	South West	10391	398	-1.47 (-1.58--1.35)	0.23 (0.21-0.26)	<1e-6
Symptoms	symptomatic	119284	8171	0	1	-
	asymptomatic	89663	6916	-0.02 (-0.06-0.02)	0.98 (0.95-1.02)	0.4348
Reinfection status	Not reinfection	206321	13586	0	1	-
	Reinfection	2626	1501	1.88 (1.79-1.97)	6.55 (5.99-7.15)	<1e-6
Hospital status	No hospital attendance	207555	15063	0	1	-
	Hospital attendance	1392	24	-0.05 (-0.49-0.39)	0.95 (0.61-1.47)	0.8275

Imperial College Report

2

Early assessment of the clinical severity of the SARS-CoV-2 Omicron variant in South Africa

Nicole Wolter, Waasila Jassat, Sibongile Walaza, Richard Welch, Harry Moultrie, Michelle Groome, Daniel Gyamfi Amoako, Josie Everatt, Jinal N Bhiman, Cathrine Scheepers, Naume Tebeila, Nicola Chiwandire, Mignon du Plessis, Nevashan Govender, Arshad Ismail, Allison Glass, Koleka Mlisana, Wendy Stevens, Florette K Treurnicht, Zinhle Makatini, Nei-yuan Hsiao, Raveen Parboosing, Jeannette Wadula, Hannah Hussey, Mary-Ann Davies, Andrew Boulle, Anne von Gottberg, Cheryl Cohen

doi: https://doi.org/10.1101/2021.12.21.21268116

Table 3 Multivariable logistic regression analysis evaluating the association between S gene target failure (SGTF) infection during 1 October – 30 November 2021, compared to Delta variant infection during April – November 2021, and severe disease among hospitalized individuals with known outcome, South Africa[a] (N=1036)

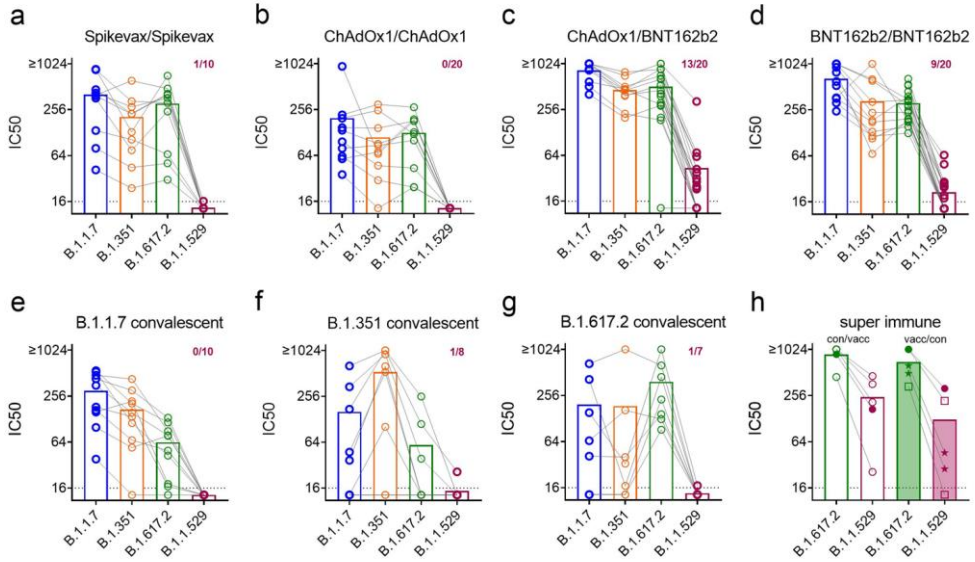
		Severe disease[b] n/N (%)	Adjusted odds ratio (95% CI)	P-value
SARS-CoV-2 variant		N=1037		
	SGTF	57/244 (23)	0.3 (0.2-0.5)	**<0.001**
	Delta	496/793 (63)	Ref	-

MedArxiv

Indicator	Red, amber or green status*	Confidence level	Assessment and rationale
Growth advantage	Red	High	**Omicron is displaying a growth advantage over Delta** This assessment is based on analysis of UK data showing increased household transmission risk, increased secondary attack rates and substantially increased growth rates compared to Delta. Omicron continues to increase as a proportion of UK cases and is now predominant in some regions of England. This growth advantage is also apparent in other countries with equivalent surveillance. The observed growth advantage may be due to immune evasion or transmissibility. Although we now have high confidence in a component of immune evasion, the very high growth rate and laboratory findings suggest that an increase in transmissibility may also be contributing.
Transmissibility	Amber	Low	**Omicron is at least as transmissible as Delta** Increased transmissibility compared to Delta is biologically plausible with the presence of furin cleavage site and nucleocapsid changes associated in vitro with advantages for replication, as well as extensive changes to the RBD. Structural modelling suggests that the mutations present may increase human ACE2 binding affinity to a much greater extent than that seen for any other variant. Early laboratory data suggest more efficient cell entry and replication in bronchial cells in vitro. However, there is no clear epidemiological demonstration of transmissibility as distinct from other contributors to growth advantage.
Immune evasion (including natural and vaccine derived immunity)	Red	High	**Omicron displays a reduction in immune protection against infection (NO data regarding severe disease)** This assessment is now based on neutralisation data from multiple laboratories, assessment of real world vaccine effectiveness in the UK and an observed increase in the risk of reinfection with Omicron. There are insufficient data to make any assessment of protection against severe disease.
Infection severity			**Insufficient data** There are insufficient data to fully assess severity, which is expected in the early period of emergence of a new variant. However, on the data available in the UK, there is no signal that supports a difference in the intrinsic virulence of the Omicron virus compared to Delta.
A separate report will be published concerning impact on therapeutics in due course.			

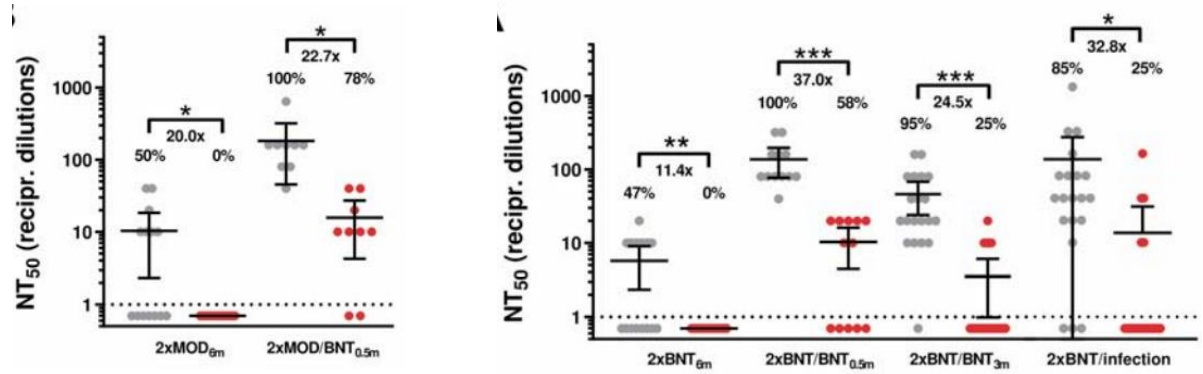
* Refer to scale and confidence grading slide

https://twitter.com/dr_d_robertson/status/1468657221085147137

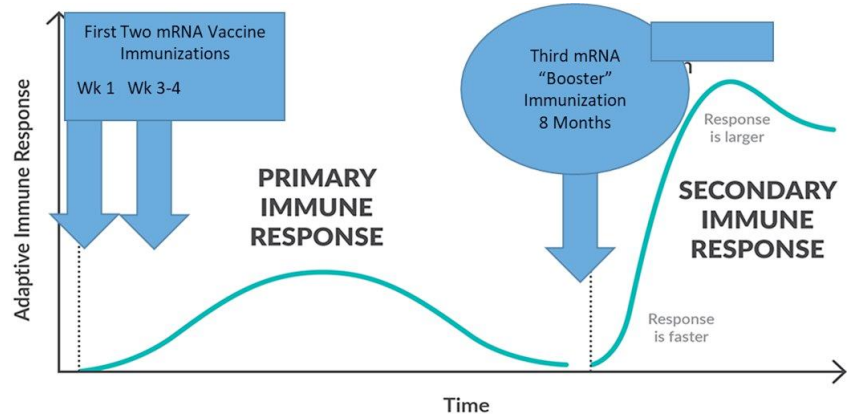


Kimpel, Medical University of Innsbruck
https://twitter.com/janinekimpel/status/1468700628922904591

Omicron Red
Delta grey



Ciesek, Institute for Medical Virology, University Hospital Frankfurt
https://www.medrxiv.org/content/10.1101/2021.12.07.21267432v1.full.pdf



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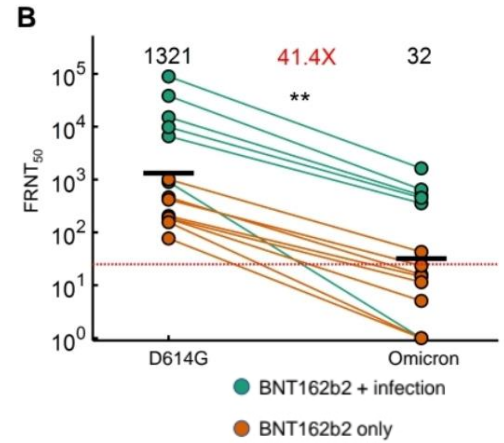

Sigal, Max Planck Institute for Infection Biology (lab in Durban (SA)
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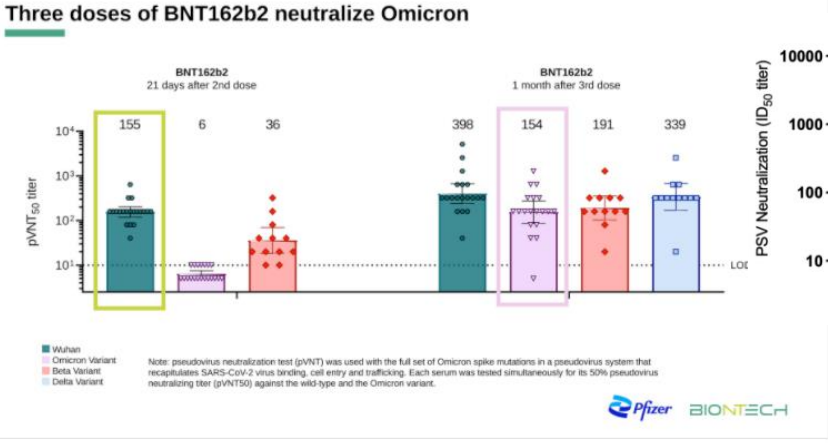
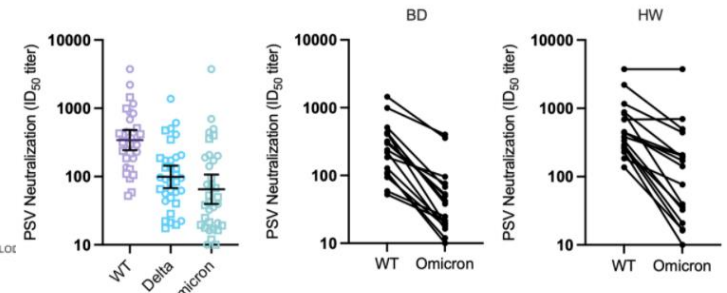


Pfizer study
https://twitter.com/EricTopol/status/1468593675747794946



Sheward, **Karolinska** Cancer Institute Sweden, Institute of Infectious Diseases and Molecular Medicine, University of Cape Town,
https://drive.google.com/file/d/1CuxmNYj5cpIuxWXhjjVmuDgntxXwlfXQ/view

15 December 2021 Risk assessment for SARS-CoV-2 variant: Omicron VOC-2

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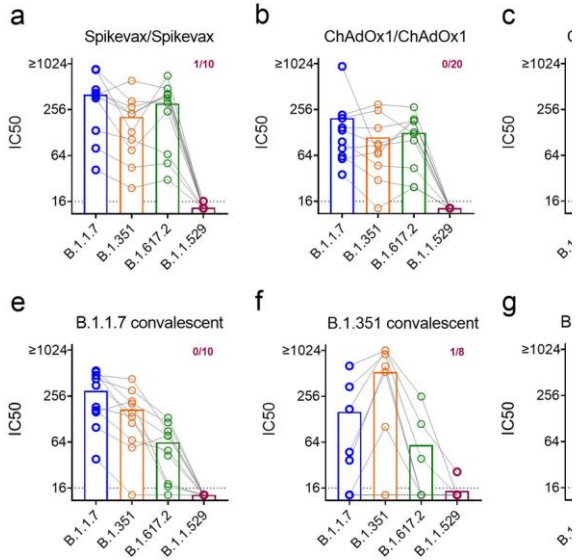
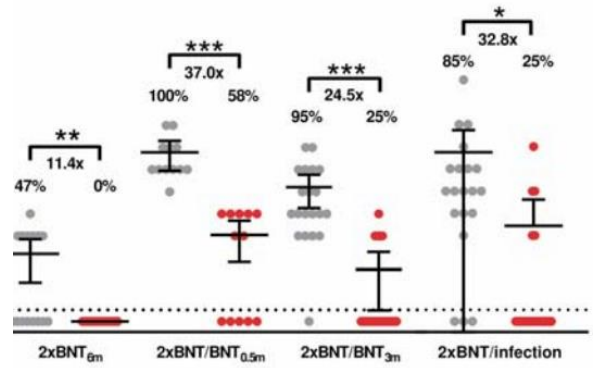


Kimpel, Medical University of Innsbruck
https://twitter.com/janinekimpel/status/1468700628922904591

Omicron neutralization studies as of Dec 12h 9:30pm GMT

Study	Virus	Sera	N	Fold reduction	Against …	Remarks	Link
Sigal	Live	Pfizer (2nd shot)	6	40x	W	Full manuscript available. Note that Omicron here had R346K	https://bit.ly/omicron2
		Recovered + Pfizer (2nd shot)	6				
Karolinska	Pseudo lenti	Random Donors	17	7x	W	Full manuscript available. The details about the vaccination type of the donors are incomplete	https://bit.ly/omicron1
		Infected	17	5x			
Ciesek	Live	Pfizer (2nd shot)	>5	>10x (wipes out everyone below LoD)	D	The number of people in each condition is unknown. The study describes more conditions	https://bit.ly/omicron3
		Pfizer (3rd shot)	>5	~30x			
		Pfizer (2nd shot+ infected)	>5	30x			
Pfizer	Pseudo	Pfizer (3rd shot)	18(o) 12(Δ)	2.5x	D	A press release.	https://bit.ly/omicron4
Kimpel	Live	Pfizer (2nd shot)	>10	~16x	D	Full manuscript is now available	https://bit.ly/omicron5
Zhang	Pseudo	Convalescent	28	8x	W	A full manuscript	https://bit.ly/omicron6
Schmidt	Pseudo	Pfizer (2nd shot) and Pfizer (3rd shot after 1m)	54 (Pfizer)	16x	W	A full manuscript. Spike includes R683G. The study describes more conditions	https://bit.ly/omicron7
Israeli MoH	Live	Pfizer (2nd shot)	?	20x	W	Just a tweet from TV for now	https://bit.ly/omicron8
		Pfizer (3rd shot 1M)	?	9x	W		https://twitter.com/erlichya/status/1470152359057764355?s=21

W: Ancestral; D: Delta
By @erlichya



ospital Frankfurt
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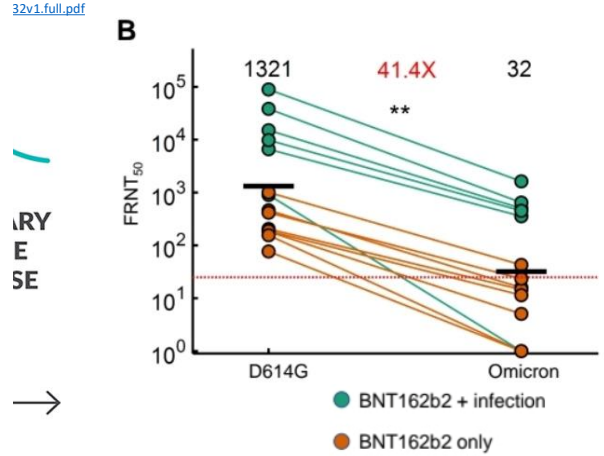

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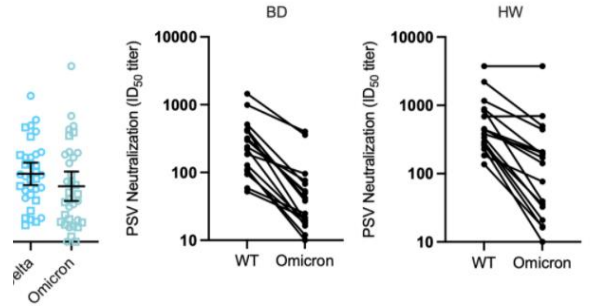

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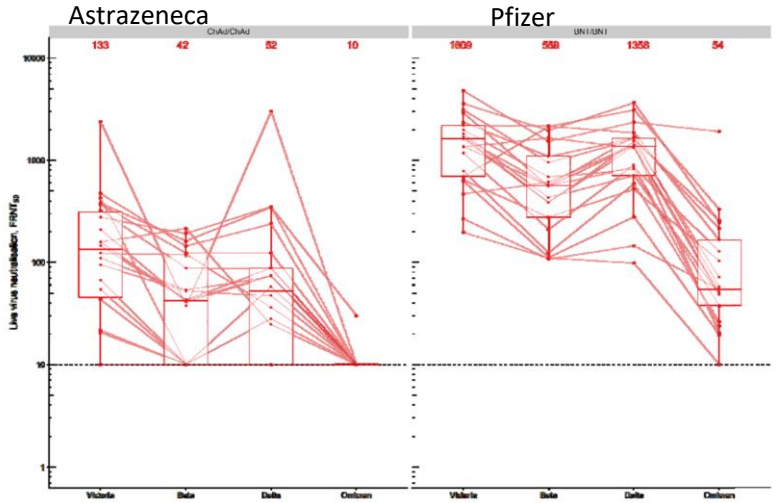
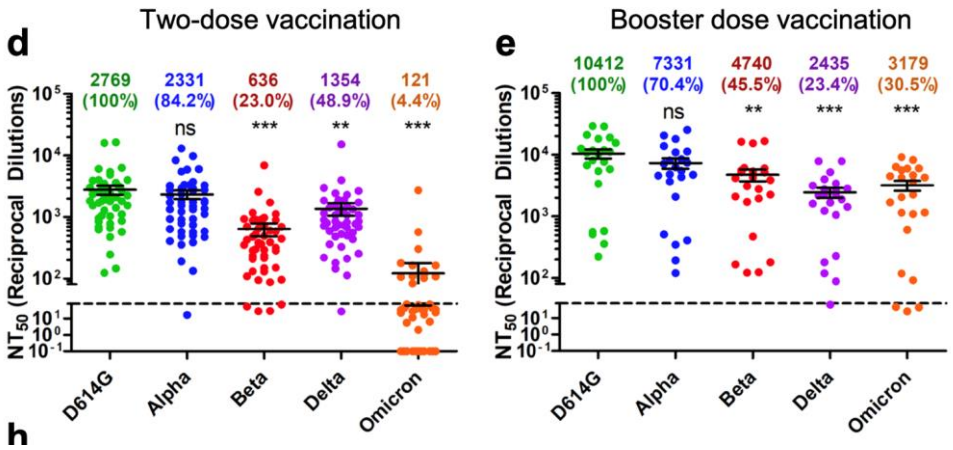
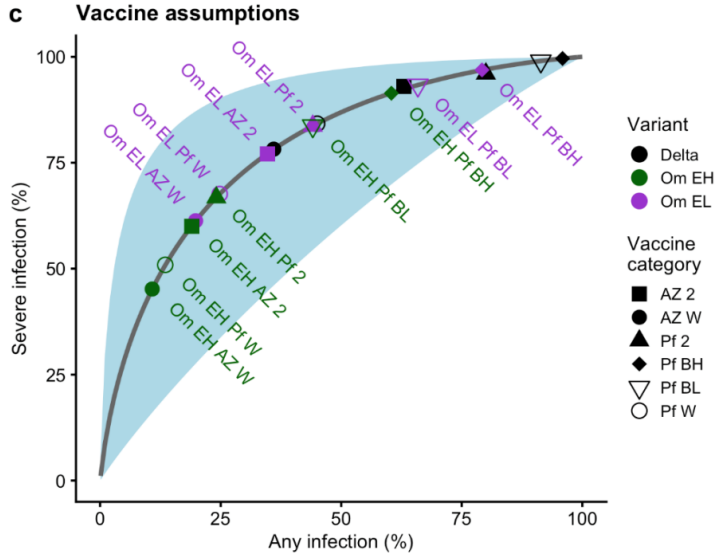
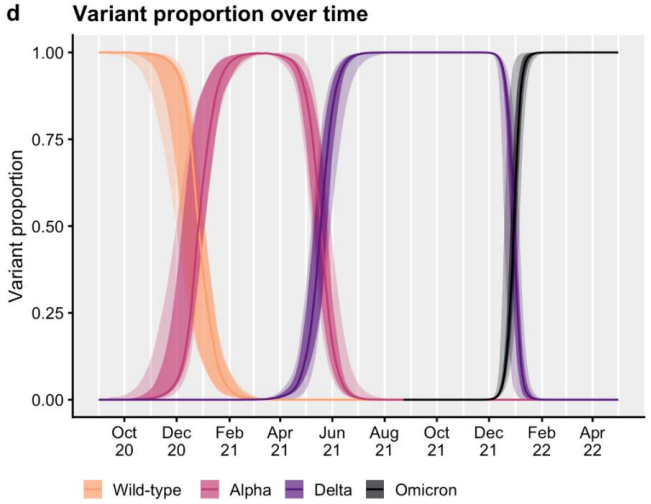


Oxford: Shows reduced live virus neutralisation of SARS-COV-2 Omicron-B.1.1.529 variant by post immunisation serum
https://www.medrxiv.org/content/10.1101/2021.12.10.21267534v1.full.pdf



Ohio State: Findings suggest dual immune evasion strategies for Omicron, due to altered epitopes and reduced exposure of the S receptor binding domain, coupled with enhanced transmissibility due to enhanced S protein stability.
https://www.biorxiv.org/content/10.1101/2021.12.16.472934v1.article-info





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https://cmmid.github.io/topics/covid19/reports/omicron_england/report_11_dec_2021.pdf

b

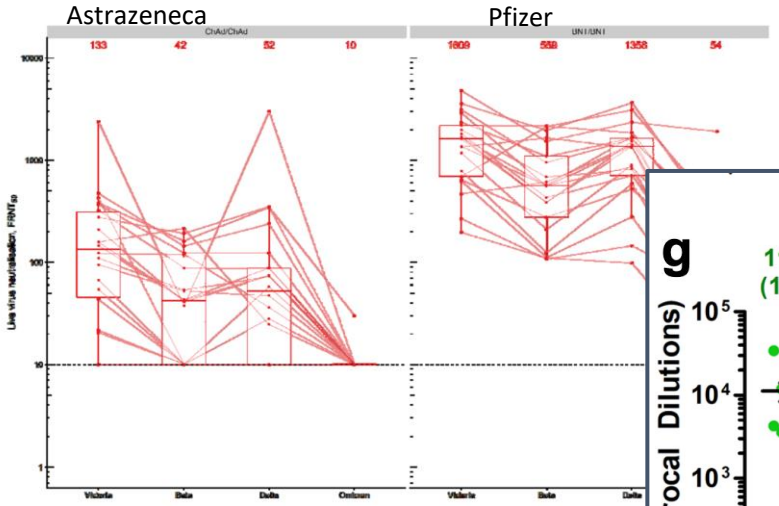
	D614G	Alpha	Gamma	Beta	Delta	Omicron
LY−CoV555	0.013	0.008	>10	>10	>10	>10
LY−CoV016	0.032	1.707	>10	>10	0.024	>10
REGN10933	0.005	0.007	0.055	0.098	0.003	>10
REGN10987	0.005	0.003	0.003	0.002	0.005	>10
AZD8895	0.001	0.002	0.012	0.014	0.002	6.860
AZD1061	0.001	0.001	0.002	0.003	0.004	>10
VIR−7831	0.058	0.080	0.066	0.050	0.073	0.181
BRII−196	0.053	0.031	0.041	0.030	0.042	7.258
DXP−604	0.010	0.007	0.005	0.065	0.016	0.287

IC50 (ng/μL)
0 5 10

c

	Antibody	BD55-3152	BD55-5319	BD55-5386	BD55-5300	BD55-3372	BD55-3500
	Epitope Group	E	E	E	F	F	F
Variants Pseudovirus IC50 (μg/mL)	D614G	0.0105	0.0150	0.0005	0.0051	0.0068	0.1053
	Beta	0.0076	0.0040	0.0011	0.0031	0.0073	0.2326
	Omicron	0.0142	0.3685	0.0584	0.0663	0.0097	0.2610
Sarbecovirus RBD ELISA (OD450)	SARS-CoV-1	3.462	3.447	3.417	3.405	3.467	3.476
Clade 1b	RaTG13	0.353	0.135	0.086	0.193	0.061	3.258
Clade 1b	Pangolin-GD	1.132	2.657	0.421	3.526	3.493	3.57
Clade 1b	Pangolin-GX	0.996	0.812	1.95	0.709	2.889	3.403
Clade 1a	SARS-CoV-1 PC4-127	3.598	3.523	3.473	3.531	3.557	3.457
Clade 1a	SARS-CoV-1 Sin852	3.458	3.495	3.468	3.464	3.413	2.984
Clade 1a	WIV1	2.409	1.976	3.336	3.588	3.515	3.603
Clade 3	BM48-31	0.133	3.424	0.115	3.483	3.515	3.476
Clade 2	YN2013	0.168	0.244	0.074	0.601	0.072	2.683

Beijing: B.1.1.529 escapes the majority of SARS-CoV-2 neutralizing antibodies of 2 diverse epitopes. 247 human anti-RBD NAbs identified from SARS41 CoV/SARS-CoV-2 convalescents and vaccinees clustered into six epitope groups (A-F). Panel b shows antibody therapeutic neutralization performance. Panel C shows Nabs Groups E & F are the most resilient wrt Omicron neutralization but they are also the most rare.
https://www.medrxiv.org/content/10.1101/2021.12.10.21267534v1.full.pdf



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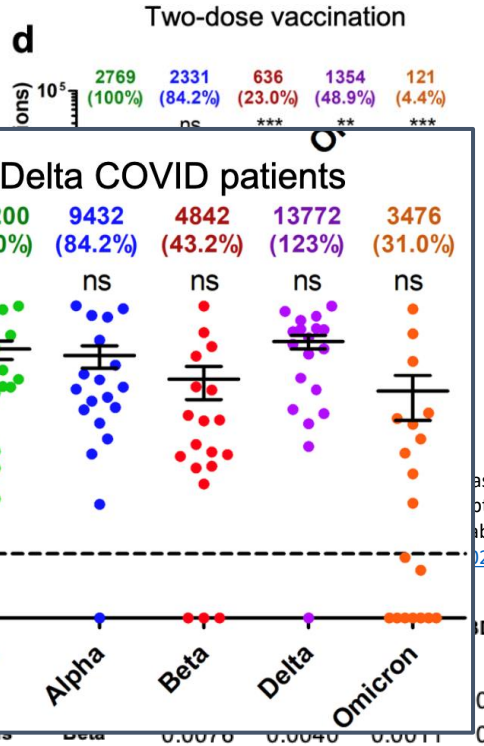

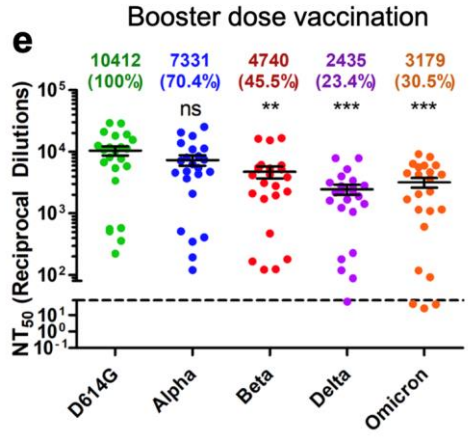

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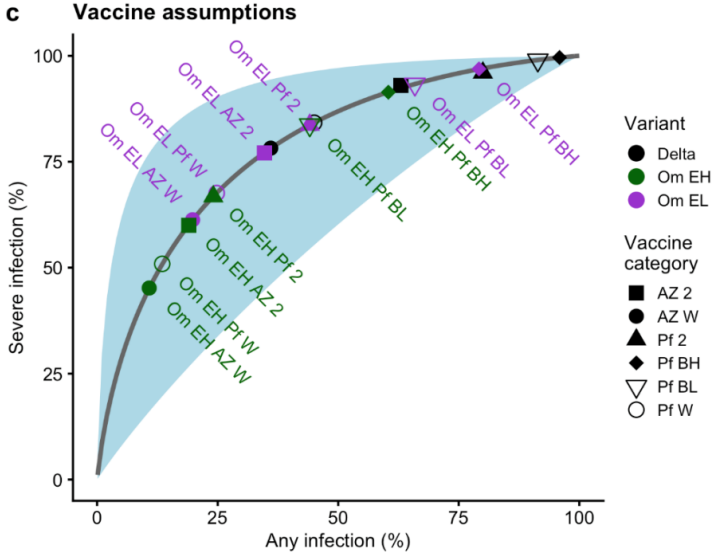

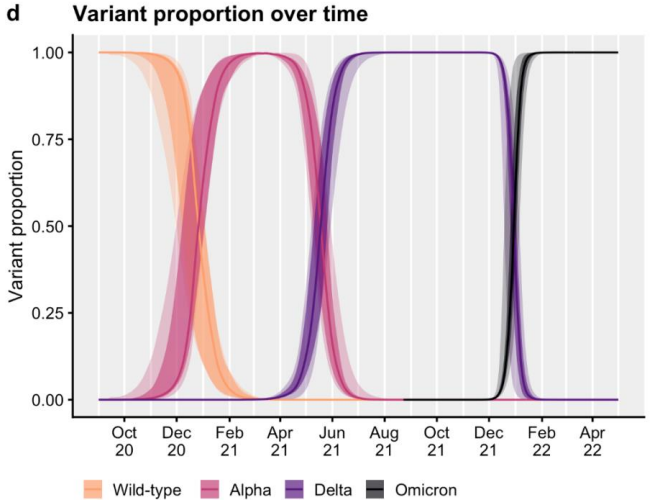

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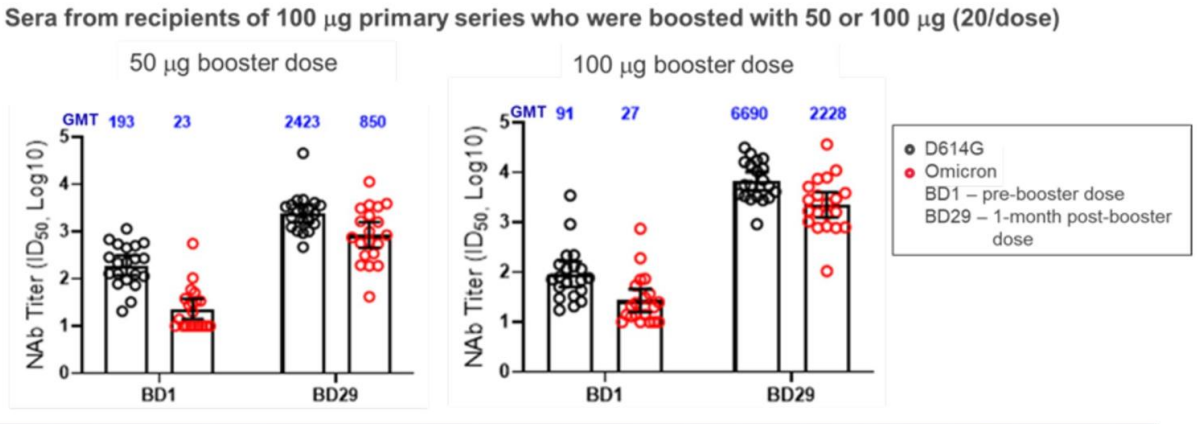
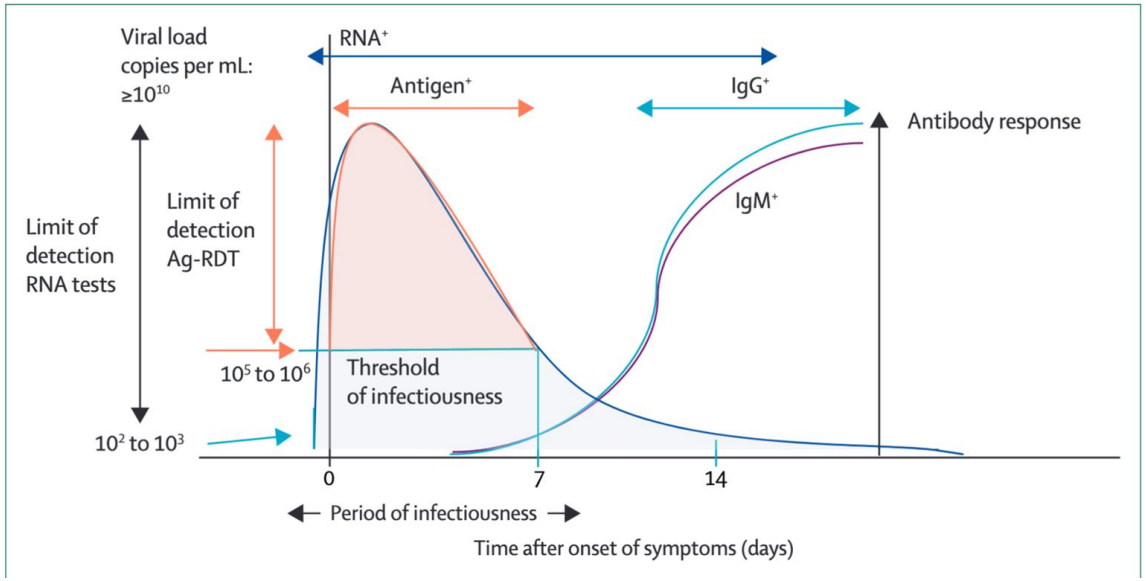
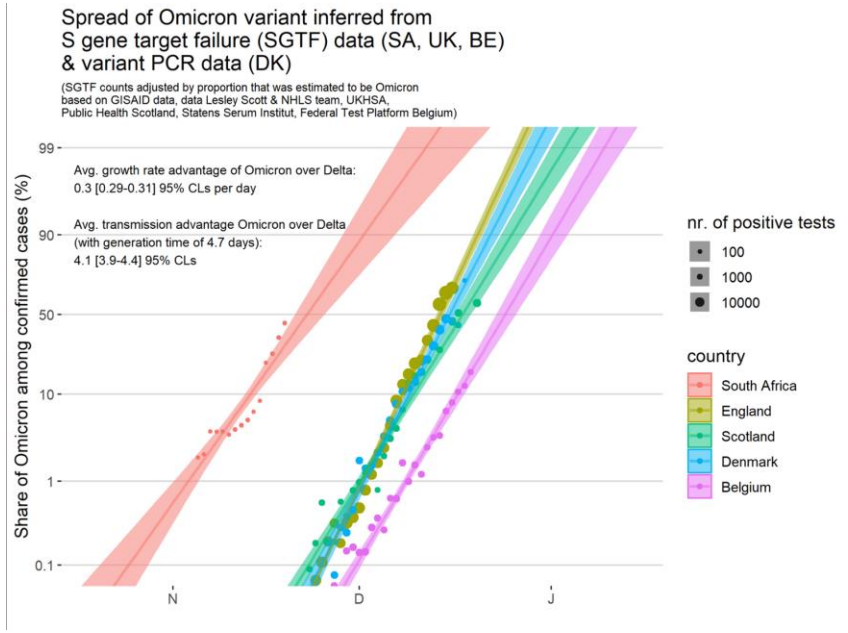
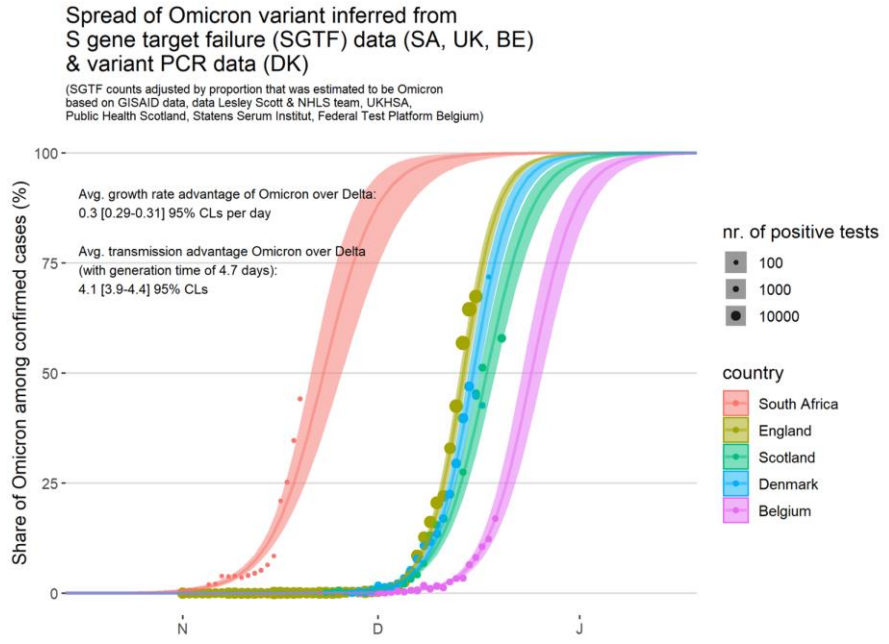


Moderna press update yesterday
https://twitter.com/erictopol/status/1472869635250814980



Evidence from 113 studies done in 17 countries shows that SARS-CoV-2 viral RNA can be detected as early as 6 days before symptom onset, concentrations peak around the time of symptom onset or a few days later, and it usually becomes undetectable from upper respiratory tract samples about 2 weeks after symptom onset, and with no substantial differences between adults and children.17 The viral load from lower respiratory tract samples might be higher, peak later, and persist for longer than the load from upper respiratory tract samples.
https://www.thelancet.com/action/showPdf?pii=S0140-6736%2821%2902346-1





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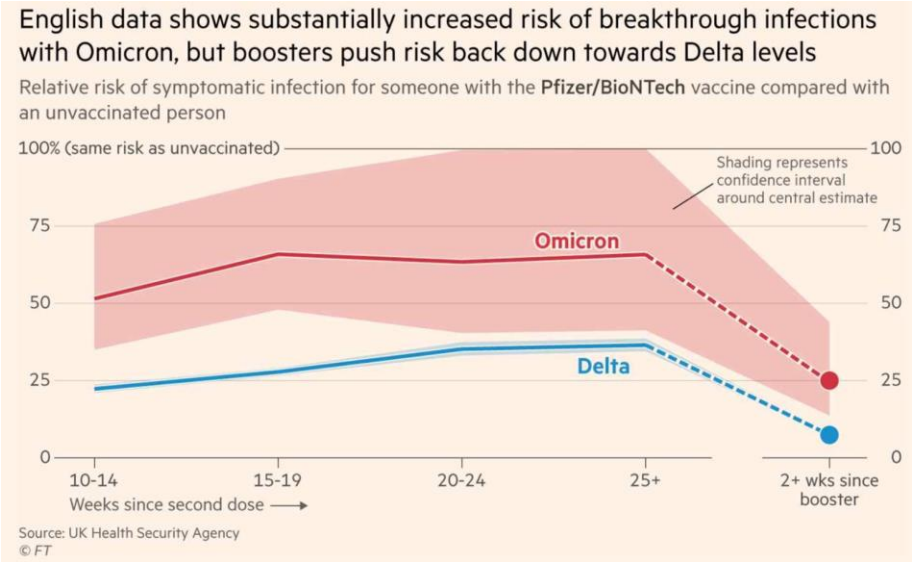
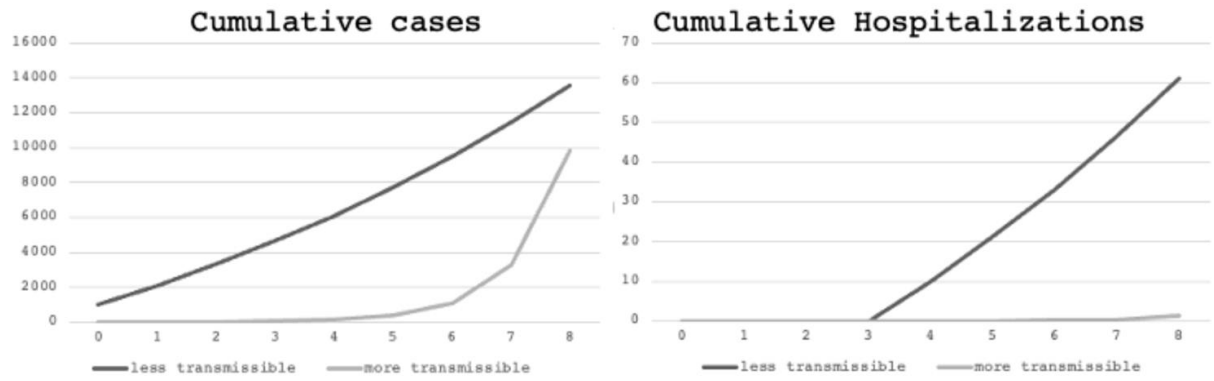


Potential to expect 5x more breakthrough cases after booster Omicron to Delta.
https://twitter.com/erlichya/status/1470759683233546244?s=21



https://twitter.com/billhanage/status/1470613668404604935?s=21

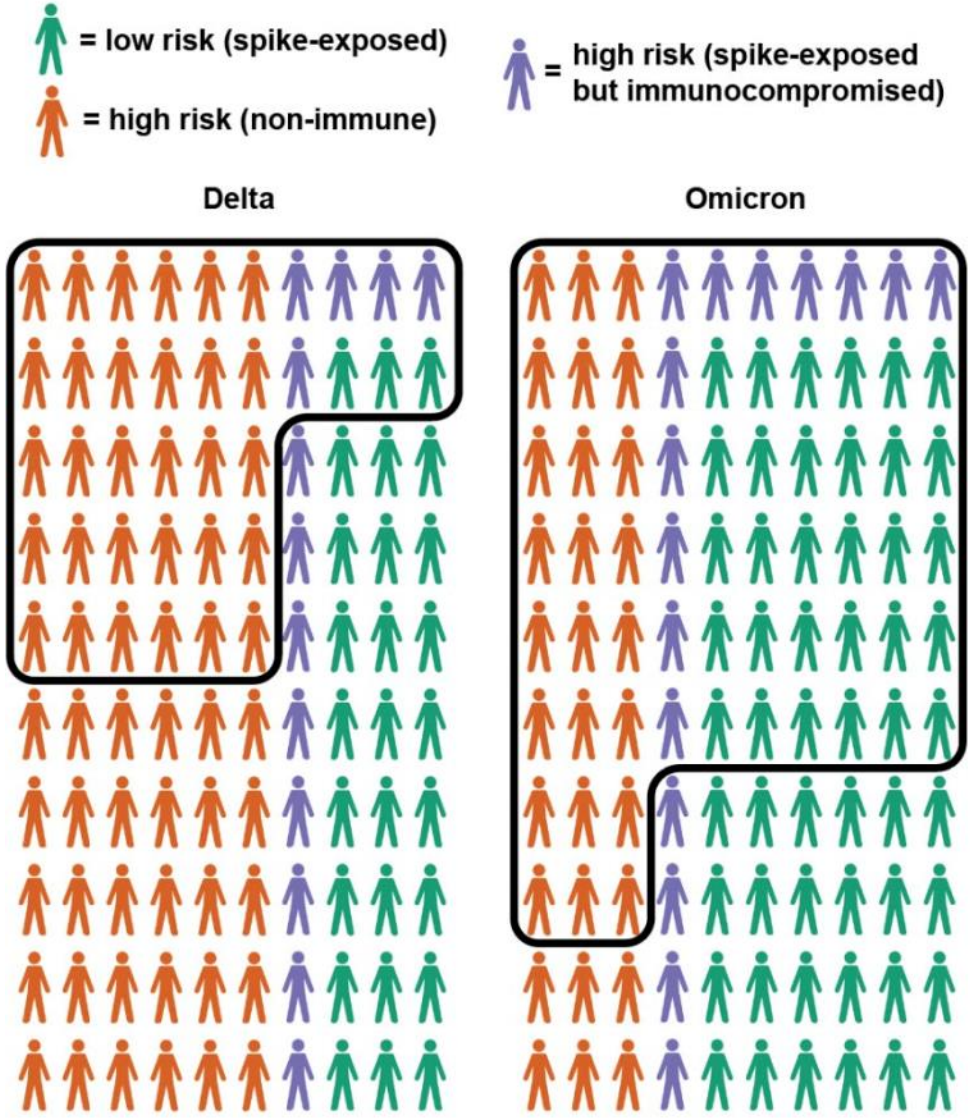


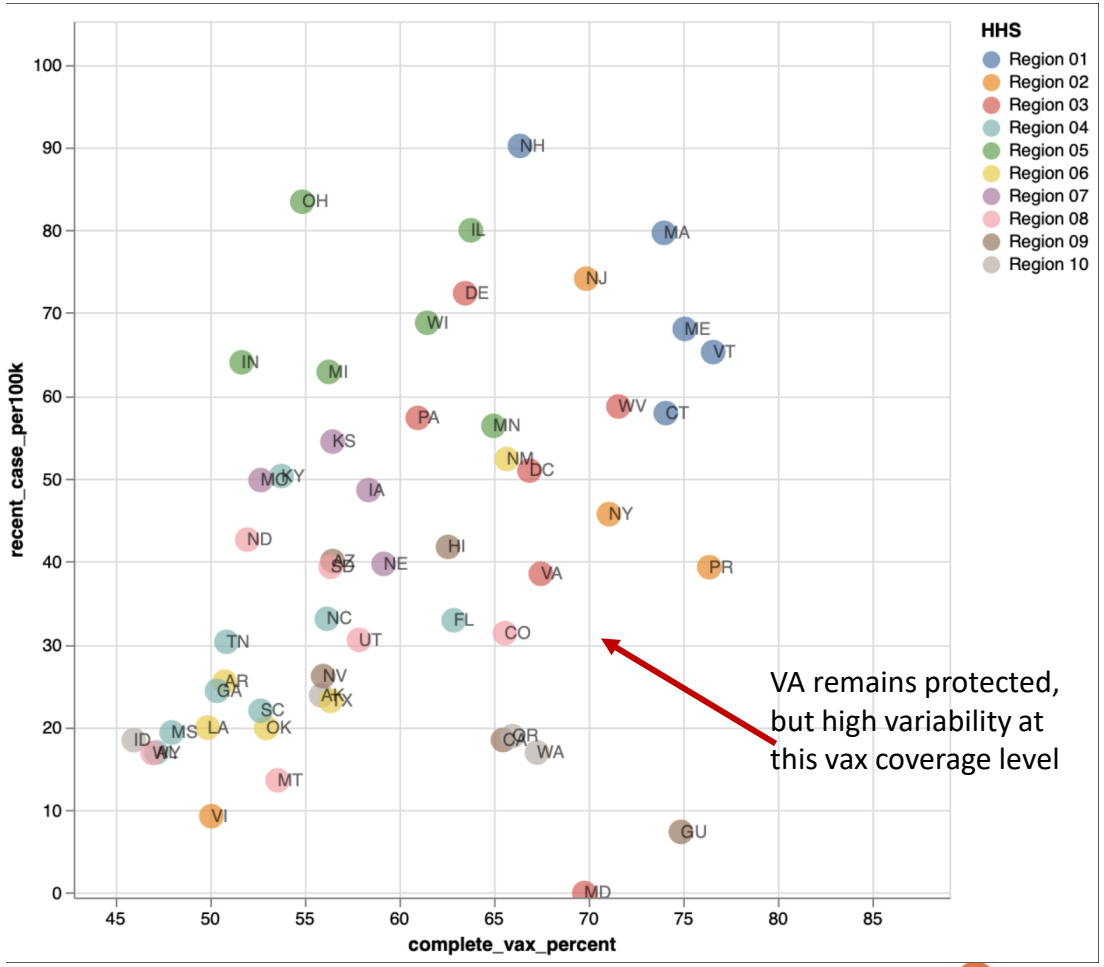
Figure 1. Challenges in comparing IFR of Omicron vs Delta

Harvard study highlights bias challenges in estimating severity
https://twitter.com/roby_bhatt/status/1471212023576870912

Recent Cases Correlate with Vax Coverage

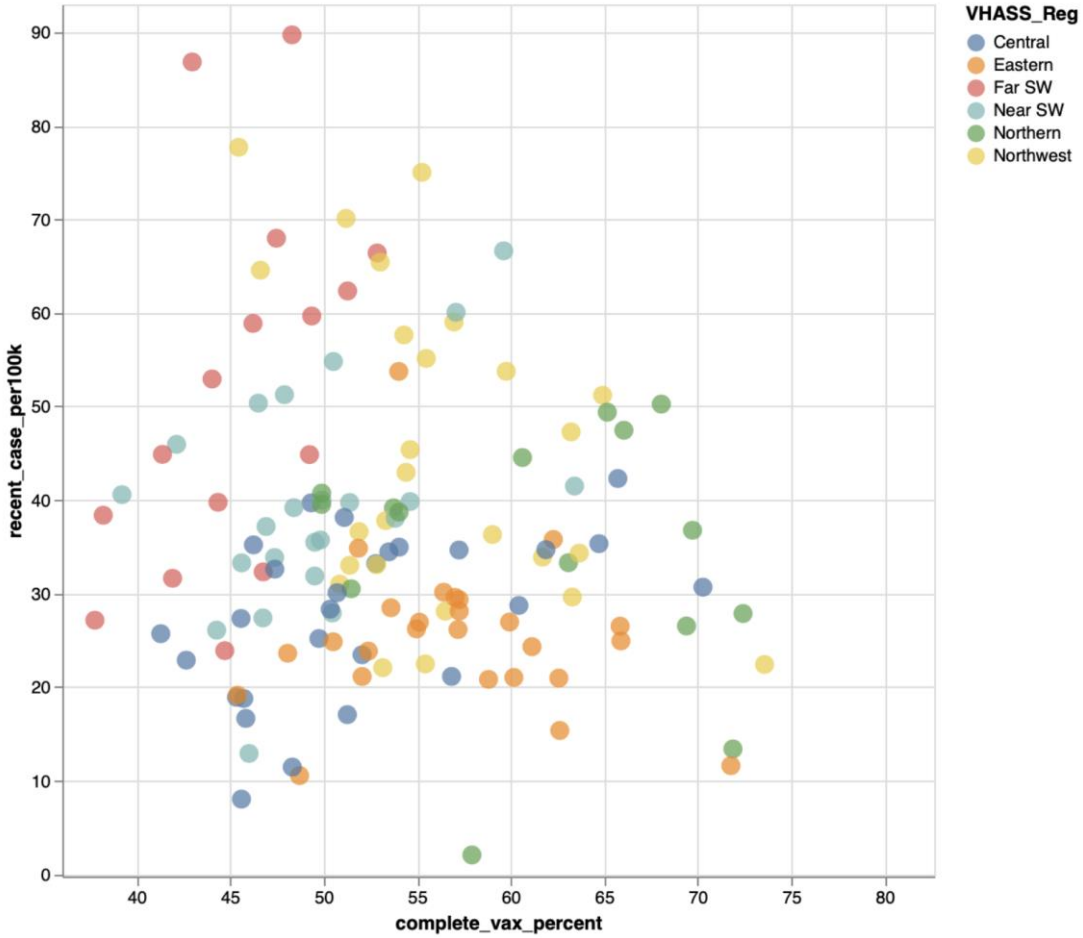
Mean cases per 100K vs. vaccine coverage

- Correlations between vax coverage and recent case rates has disappeared as more high coverage states have high rates



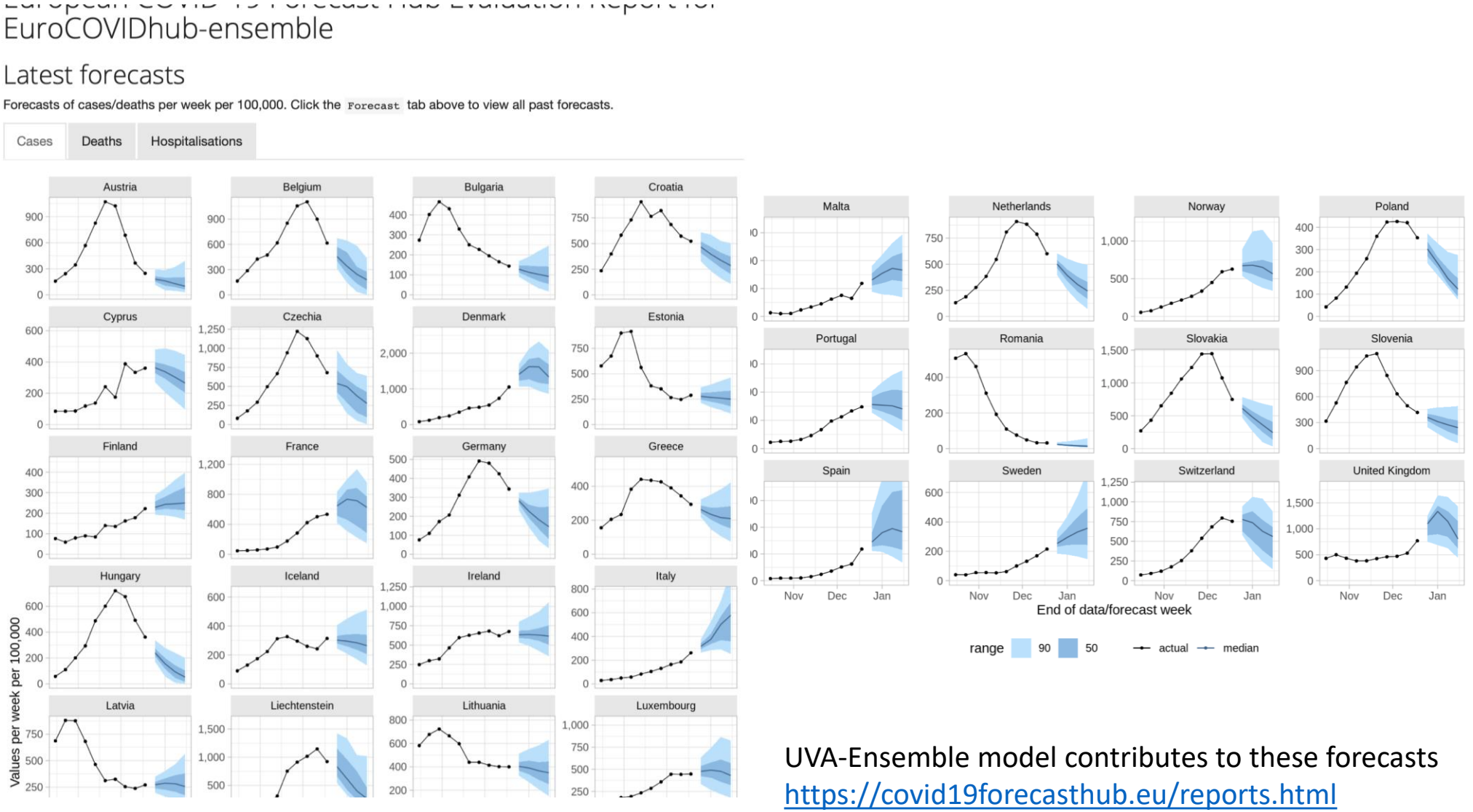
Virginia Counties

- Counties with higher vax coverage slightly lower rates



European Nations

- Case Rate changes are mixed in Europe with many countries growing rapidly while other decline
- Growth and high rates in most nations reporting significant prevalence of Omicron



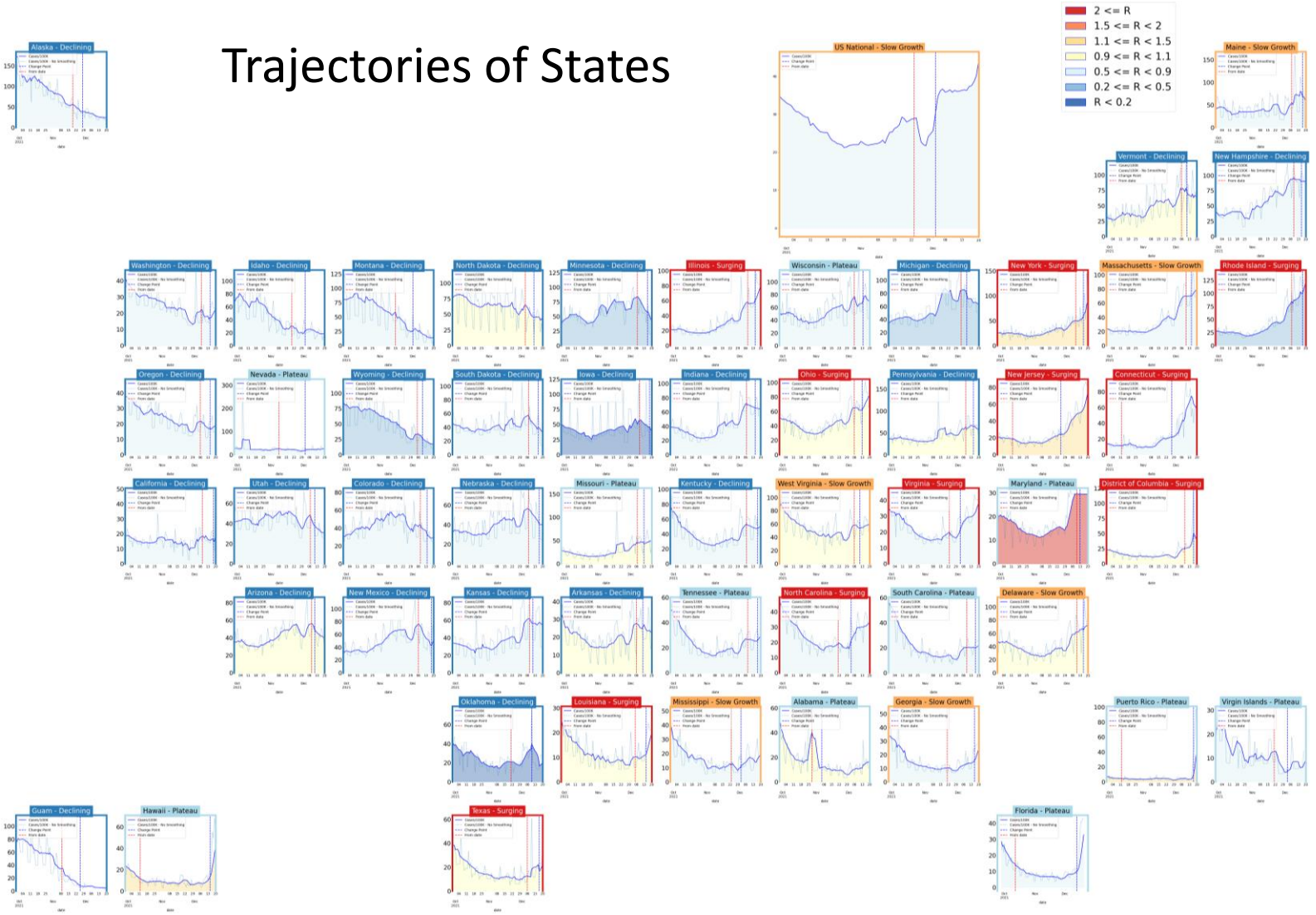
UVA-Ensemble model contributes to these forecasts
https://covid19forecasthub.eu/reports.html

United States Overall

- Overall growth has paused
- Significant number of states remain in growth
- Case rates remain moderate to high in most states

Status	# States (1 week ago)
Declining	26 (22)
Plateau	11 (13)
Slow Growth	6 (5)
In Surge	11 (14)

Trajectories of States



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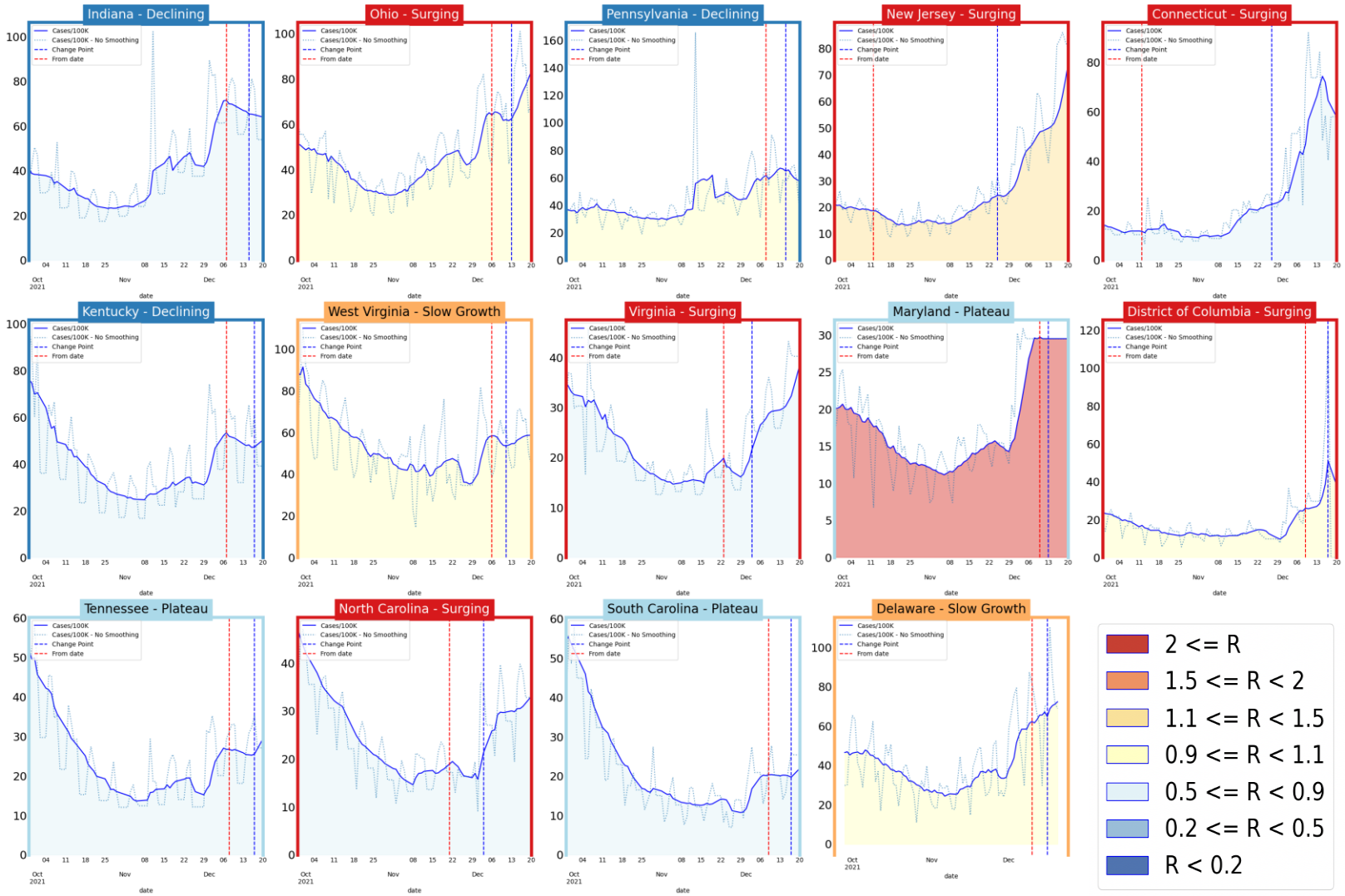
Virginia and Her Neighbors

- Recent case rate growth seems have paused in VA and most neighbors
- Case rates remain high as arrival of Omicron may fuel more growth



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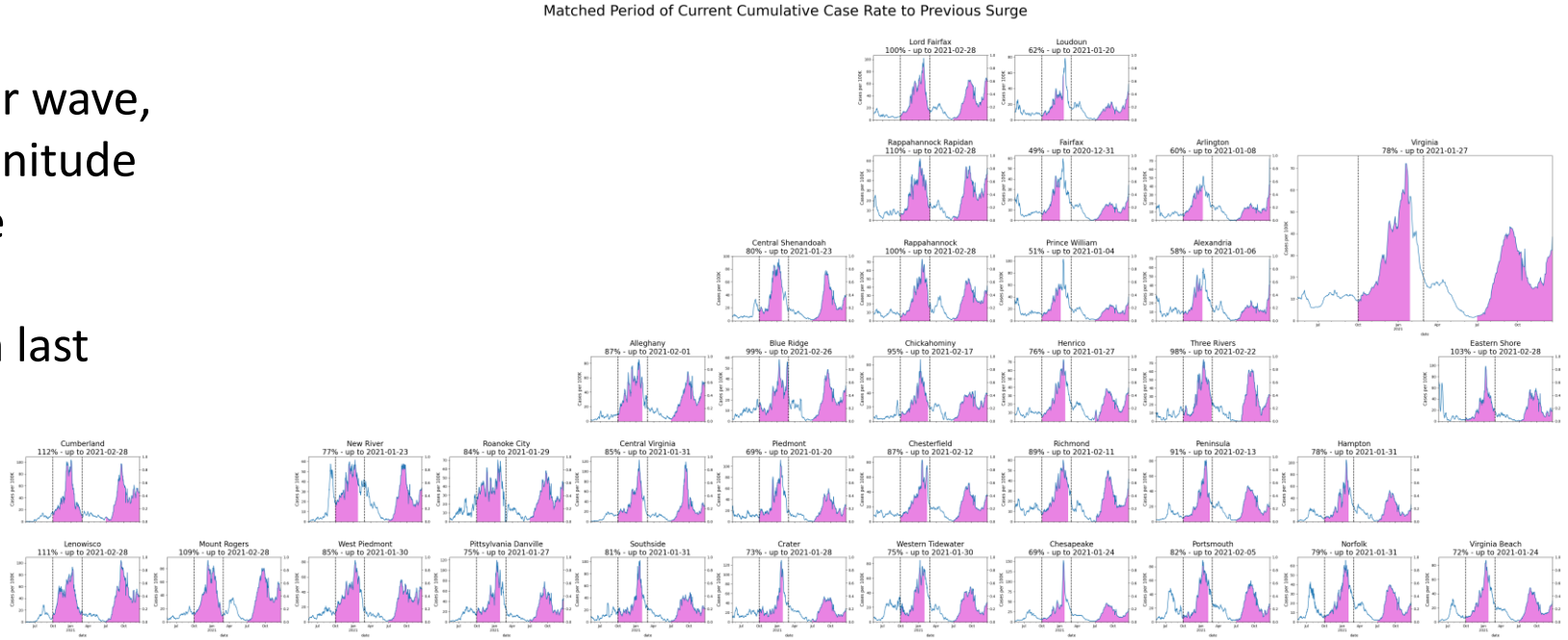
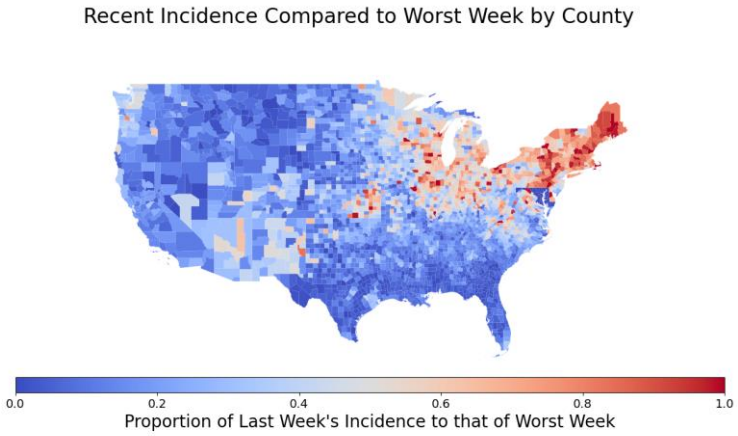
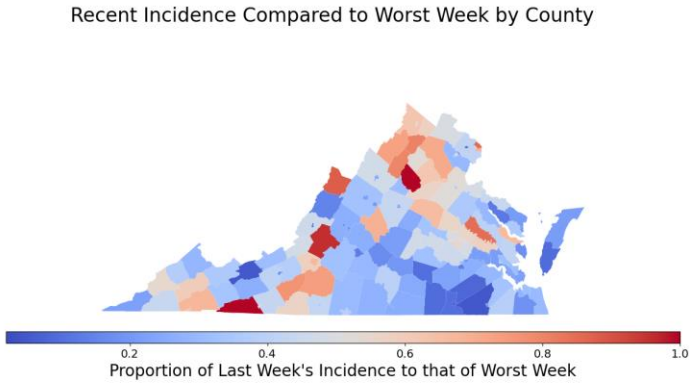
Virginia and Her Neighbors

- Current Delta and Fall- Winter wave, quickly approach overall magnitude of last years Fall-Winter wave
- Many districts have already experienced more cases than last year's Fall-Winter







- Some Counties approaching and experiencing the worst week of the pandemic this last week
- Nationally worst weeks are concentrated in Northeast

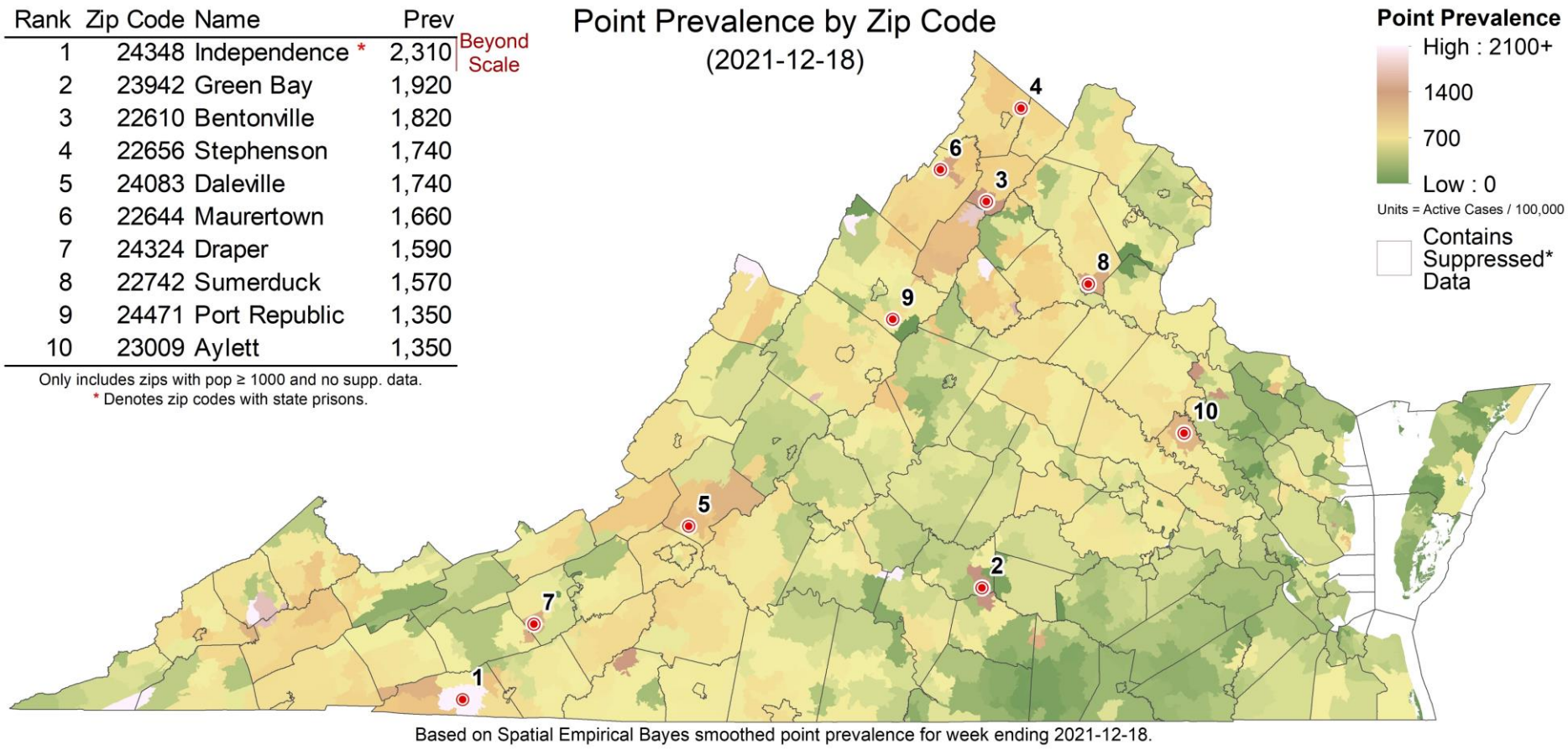
Zip code level weekly Case Rate (per 100K)

Case Rates in the last week by zip code

- Color scaled adjusted to accommodate the very high prevalence levels this week
- Clusters of high prevalence in Southwest and Northwest
- Some counts are low and suppressed to protect anonymity, those are shown in white

Rank	Zip Code	Name	Prev	
1	24348	Independence *	2,310	Beyond Scale
2	23942	Green Bay	1,920	
3	22610	Bentonville	1,820	
4	22656	Stephenson	1,740	
5	24083	Daleville	1,740	
6	22644	Maurertown	1,660	
7	24324	Draper	1,590	
8	22742	Sumerduck	1,570	
9	24471	Port Republic	1,350	
10	23009	Aylett	1,350	

Only includes zips with pop ≥ 1000 and no supp. data.
* Denotes zip codes with state prisons.



Based on Spatial Empirical Bayes smoothed point prevalence for week ending 2021-12-18.

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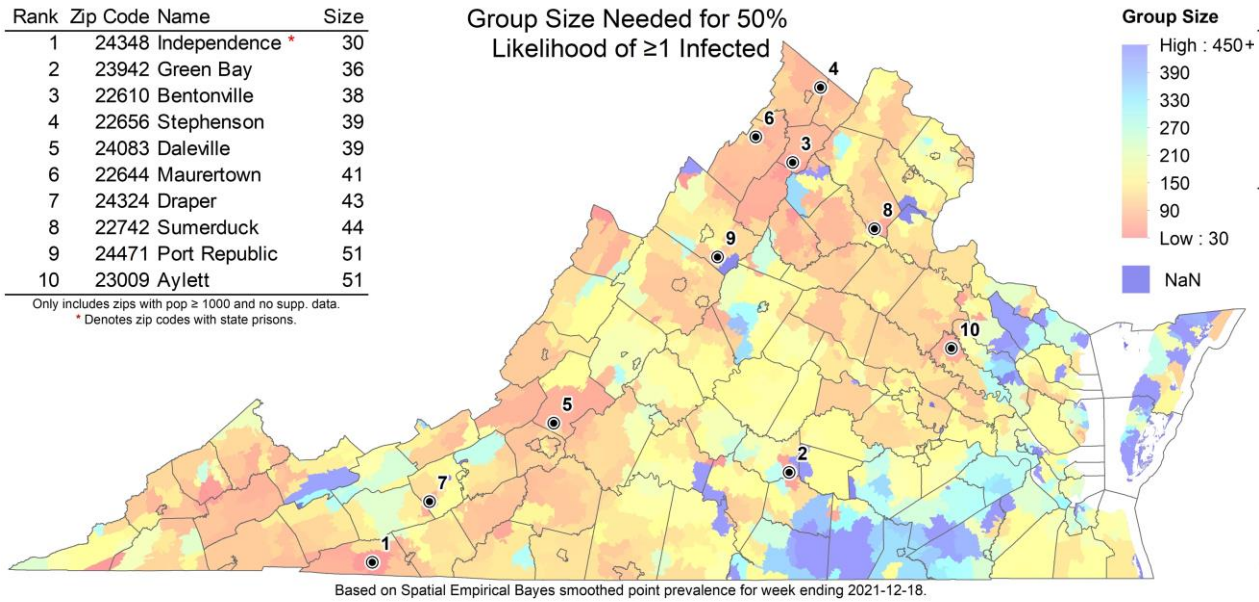
Risk of Exposure by Group Size and HCW prevalence

Case Prevalence in the last week by zip code used to calculate risk of encountering someone infected in a gathering of randomly selected people (group size 25)

- **Group Size**: Assumes 2 undetected infections per confirmed case (ascertainment rate from recent seroprevalence survey), and shows minimum size of a group with a 50% chance an individual is infected by zip code (eg in a group of 30 in Stephenson, there is a 50% chance someone will be infected)
- **HCW ratio**: Case rate among health care workers (HCW) in the last week using patient facing health care workers as the denominator / general population's case prevalence

Rank	Zip Code	Name	Size
1	24348	Independence *	30
2	23942	Green Bay	36
3	22610	Bentonville	38
4	22656	Stephenson	39
5	24083	Daleville	39
6	22644	Maurertown	41
7	24324	Draper	43
8	22742	Sumerduck	44
9	24471	Port Republic	51
10	23009	Aylett	51

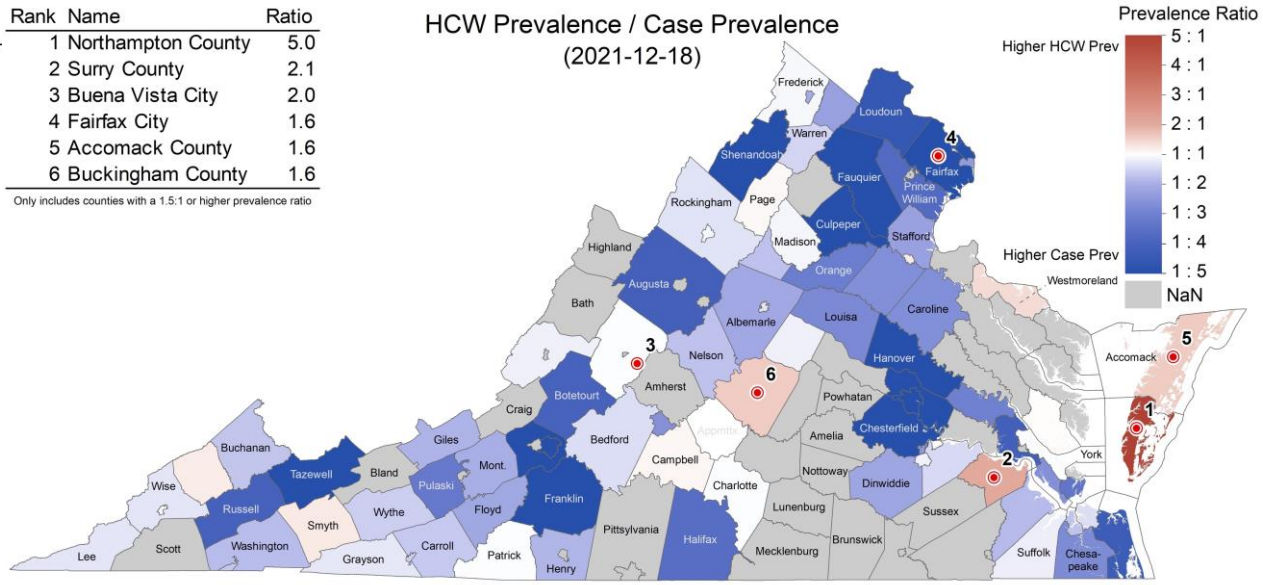
Only includes zips with pop ≥ 1000 and no supp. data.
* Denotes zip codes with state prisons.



Based on Spatial Empirical Bayes smoothed point prevalence for week ending 2021-12-18.

Rank	Name	Ratio
1	Northampton County	5.0
2	Surry County	2.1
3	Buena Vista City	2.0
4	Fairfax City	1.6
5	Accomack County	1.6
6	Buckingham County	1.6

Only includes counties with a 1.5:1 or higher prevalence ratio



Current Hot-Spots

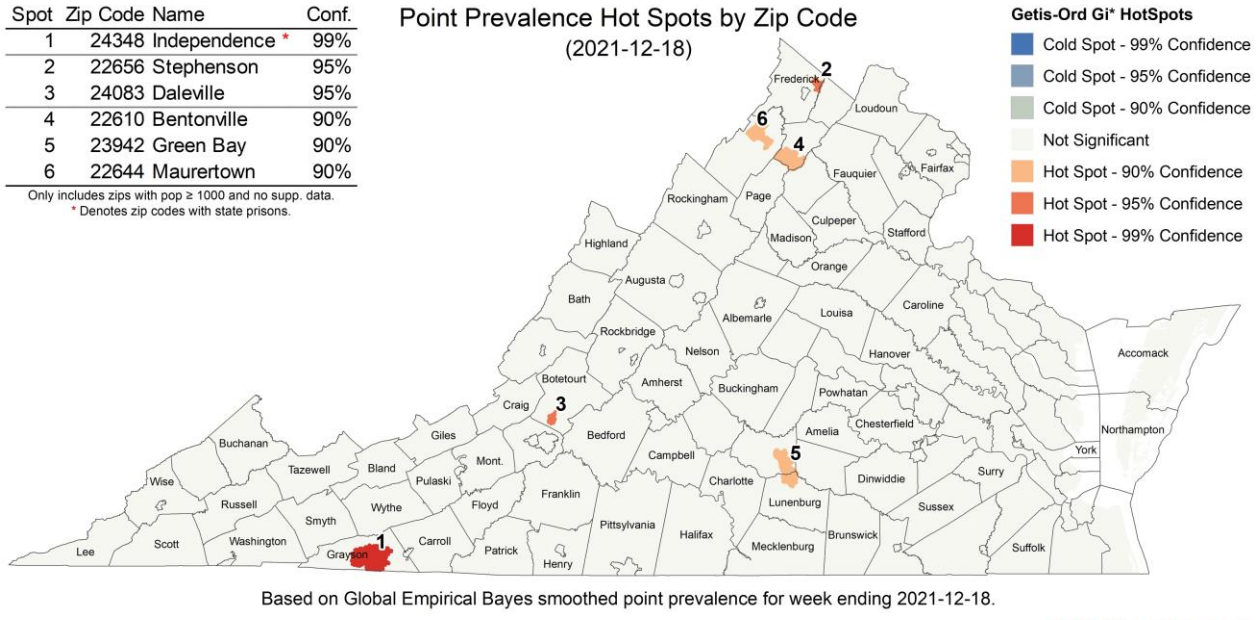
Case rates that are significantly different from neighboring areas or model projections

- **Spatial**: Getis-Ord Gi* based hot spots compare clusters of zip codes with weekly case prevalence higher than nearby zip codes to identify larger areas with statistically significant deviations
- **Temporal**: The weekly case rate (per 100K) projected last week compared to observed by county, which highlights temporal fluctuations that differ from the model's projections

Spatial Hotspots

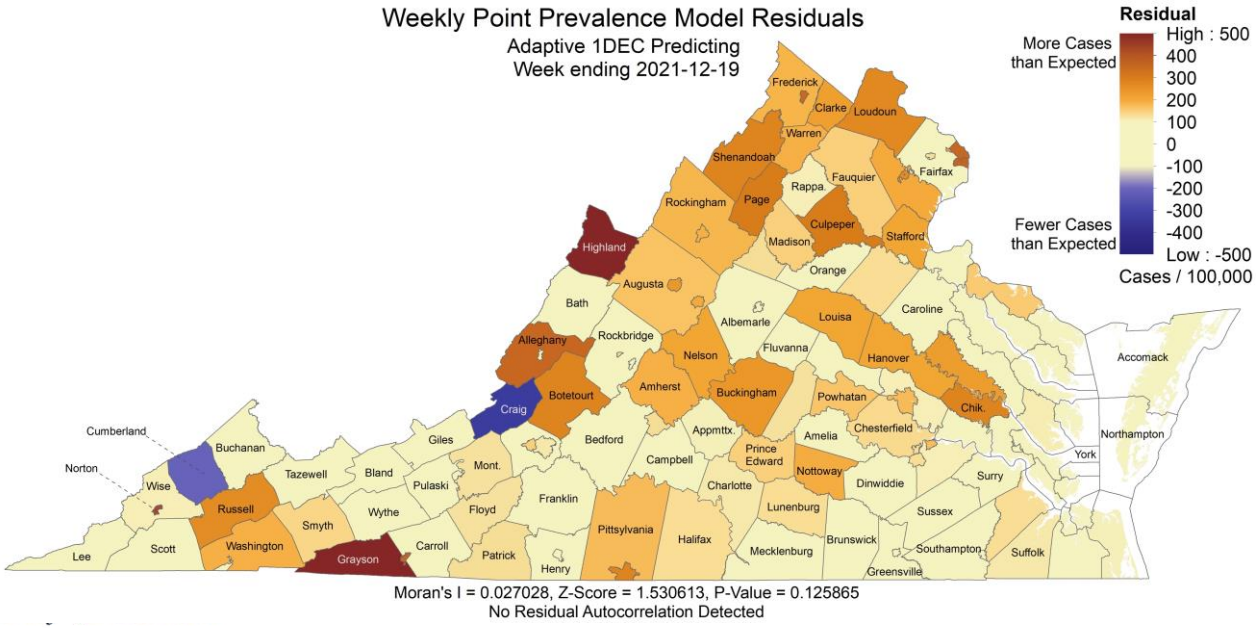
Spot	Zip Code	Name	Conf.
1	24348	Independence *	99%
2	22656	Stephenson	95%
3	24083	Daleville	95%
4	22610	Bentonville	90%
5	23942	Green Bay	90%
6	22644	Maurertown	90%

Only includes zips with pop ≥ 1000 and no supp. data.
* Denotes zip codes with state prisons.



Based on Global Empirical Bayes smoothed point prevalence for week ending 2021-12-18.

Clustered Temporal Hotspots

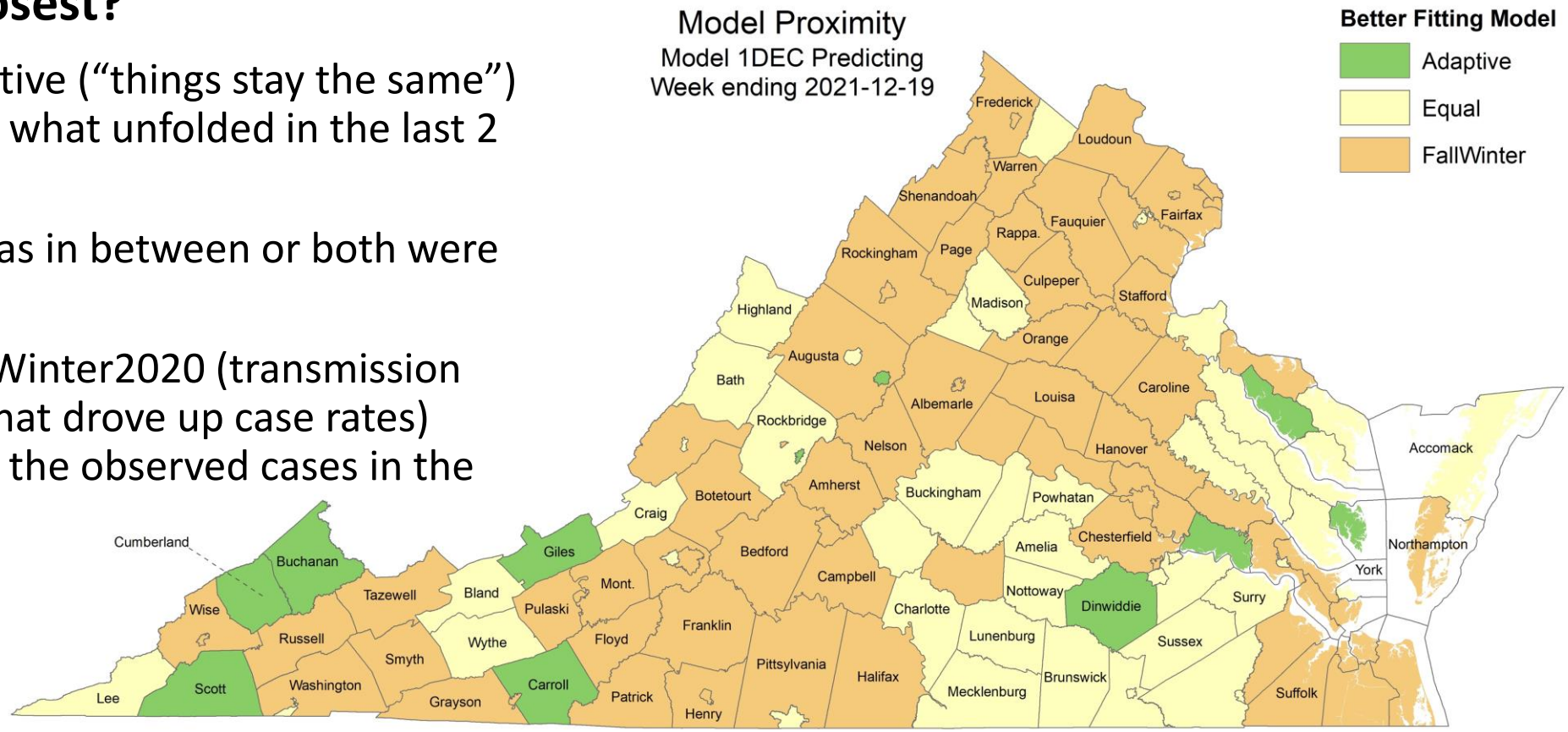


Moran's I = 0.027028, Z-Score = 1.530613, P-Value = 0.125865
No Residual Autocorrelation Detected

Scenario Trajectory Tracking

Which scenario from last projection did each county track closest?

- Green means the Adaptive (“things stay the same”) scenario was closest to what unfolded in the last 2 weeks
- Yellow means reality was in between or both were very similar
- Orange means the FallWinter2020 (transmission drivers from last year that drove up case rates) scenario was closest to the observed cases in the last 2 weeks

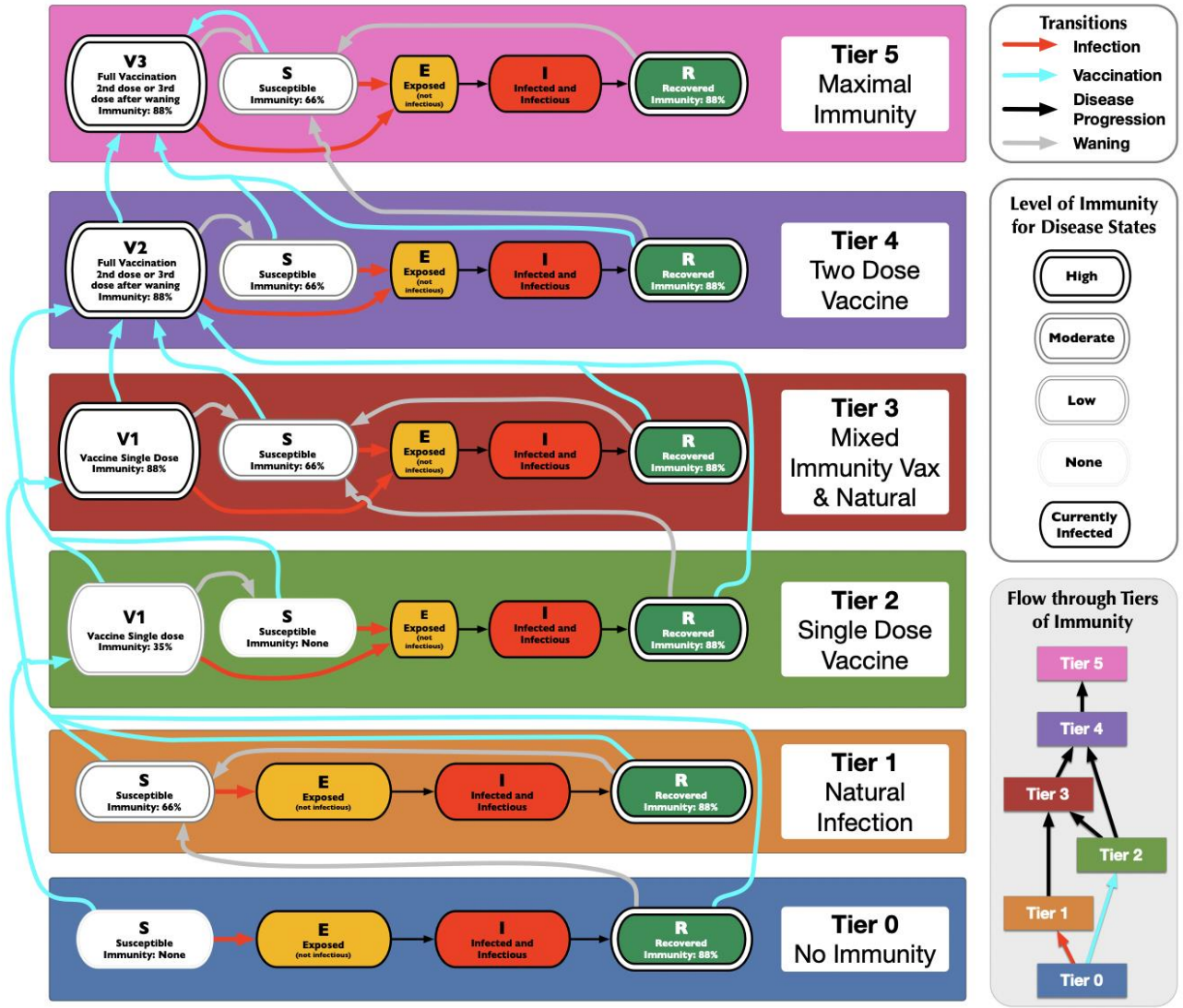


Model Update – Adaptive Fitting

New Model Structure Focused on Tiers of Immunity

Uncertainty surrounds the rate of waning immunity

- New model structure built to better track levels and timing of waning
- Outcomes vary based on age and immune history; for partial immunity, protection against hospitalization and death is stronger than No Immunity but weaker than Maximal Immunity
- Use same Adaptive fitting approach with vaccine schedules and simulated infections driving movement across the tiers
- Different Scenarios can also be applied



Adaptive Fitting Approach

Each county fit precisely, with recent trends used for future projection

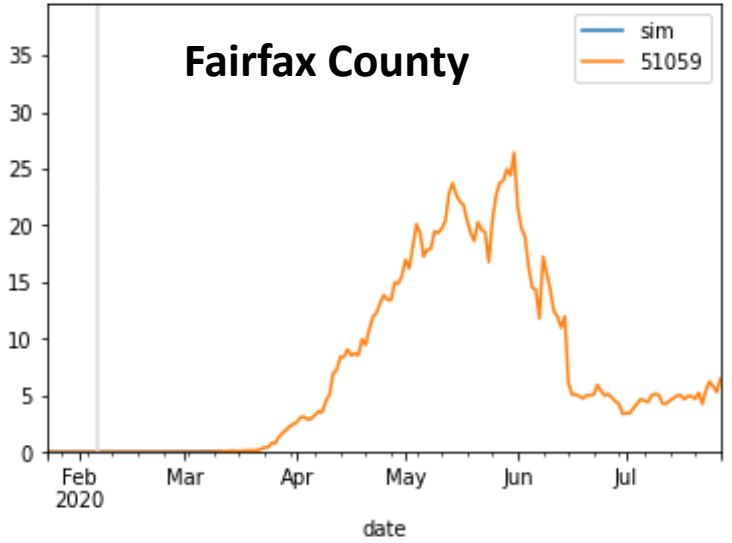
- Allows history to be precisely captured, and used to guide bounds on projections

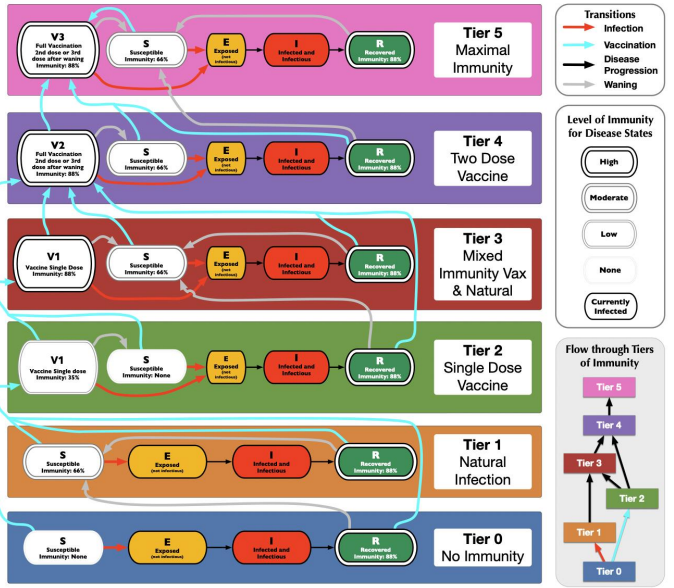
Model: An alternative use of the same meta-population model, PatchSim with multiple tiers of immunity

- Allows for future "what-if" Scenarios to be layered on top of calibrated model
- Allows for waning of immunity and for partial immunity against different outcomes (eg lower protection for infection than death)

External Seeding: Steady low-level importation

- Widespread pandemic eliminates sensitivity to initial conditions, we use steady 1 case per 10M population per day external seeding





Using Ensemble Model to Guide Projections

Ensemble methodology that combines the Adaptive v… machine learning and statistical models such as:

- Autoregressive (AR, ARIMA)
- Neural networks (LSTM)
- Kalman filtering (EnKF)

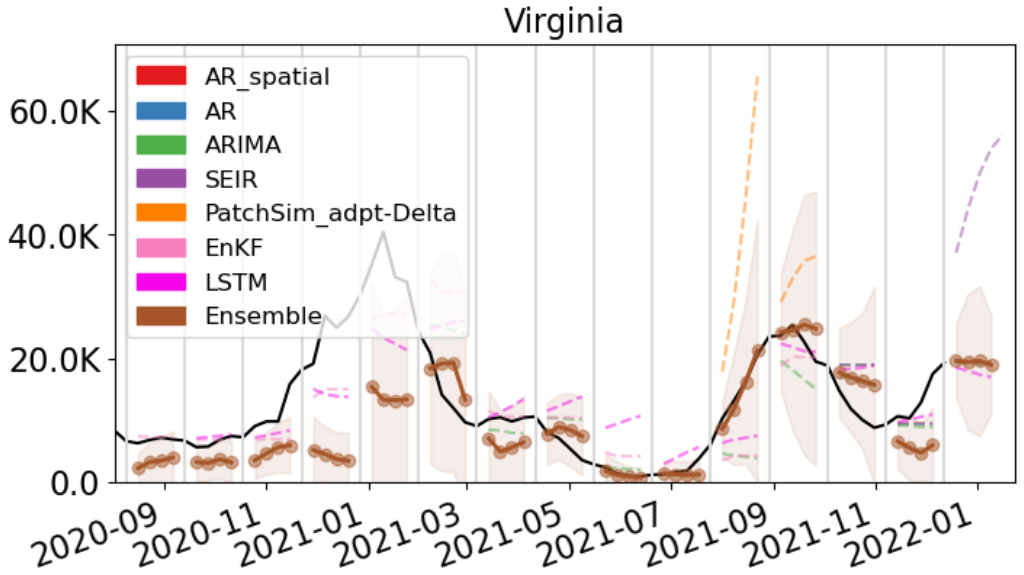
Weekly forecasts done at co… el.

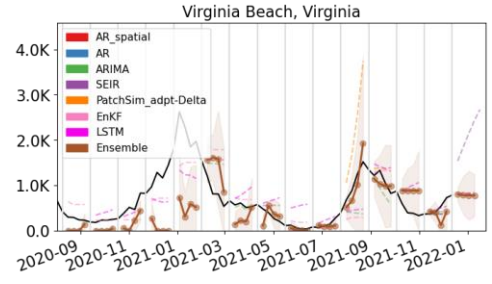
Models chosen because… track record in disease forecasting and to in… iversity and robustness.

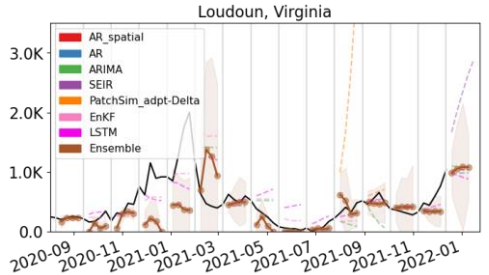
Ensemble fore… vides additional 'surveillance' for making sce… ased projections.

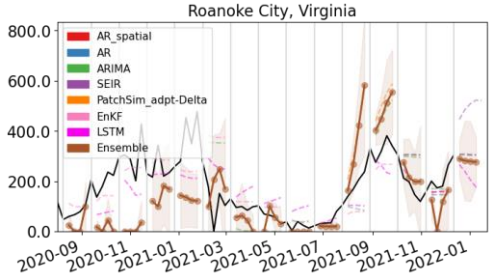
Also su… itted to CDC Forecast Hub.

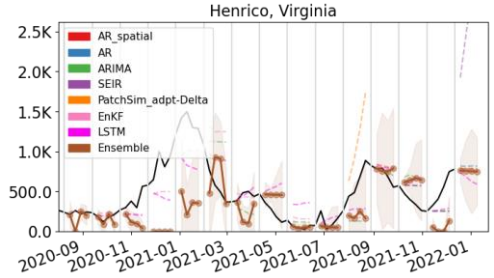
Ensemble not calibrated to Omicron therefore not used for this week's projections
Plots updated for additional situational awareness











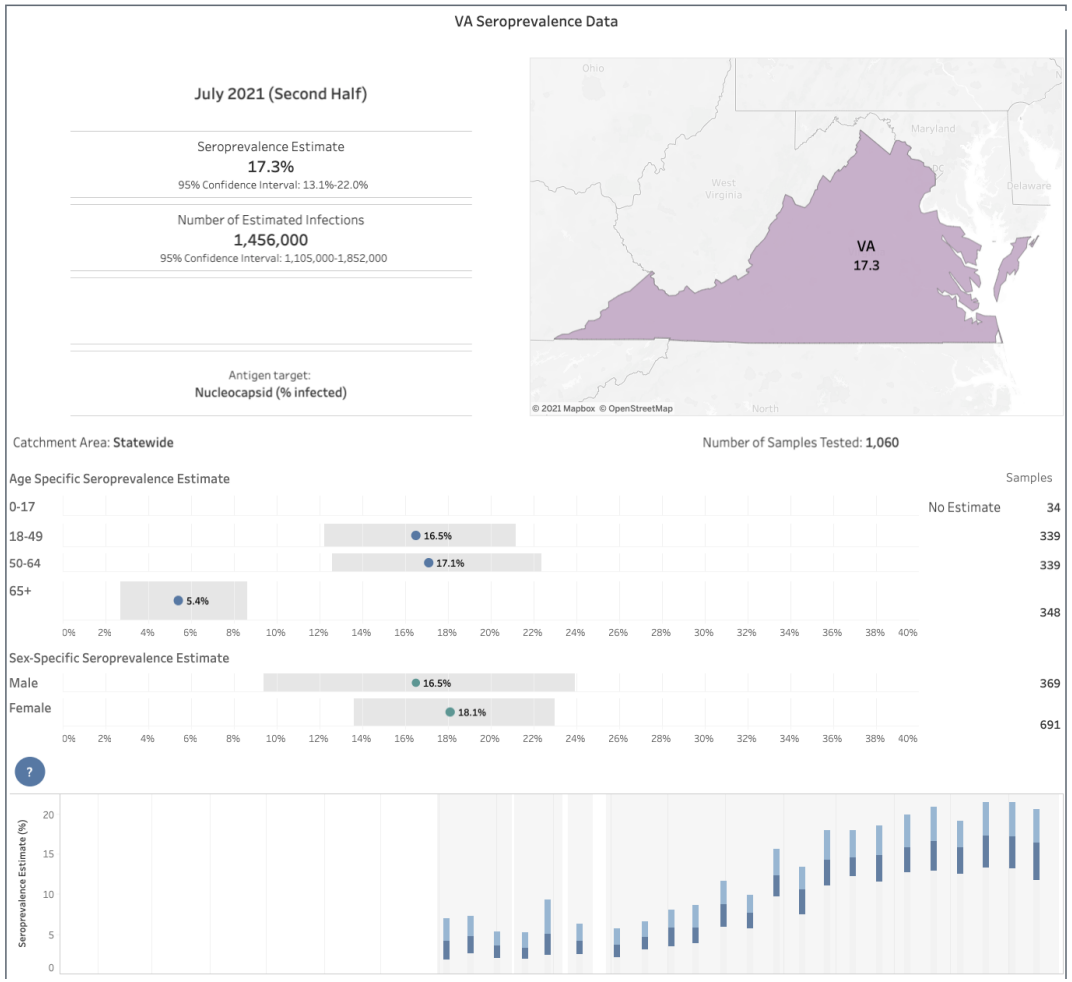
Seroprevalence updates to model design

Several seroprevalence studies provide better picture of how many actual infections have occurred

- CDC Nationwide Commercial Laboratory Seroprevalence Survey

These findings are equivalent to an ascertainment ratio of ~2x in the future, with bounds of (1.3x to 3x)

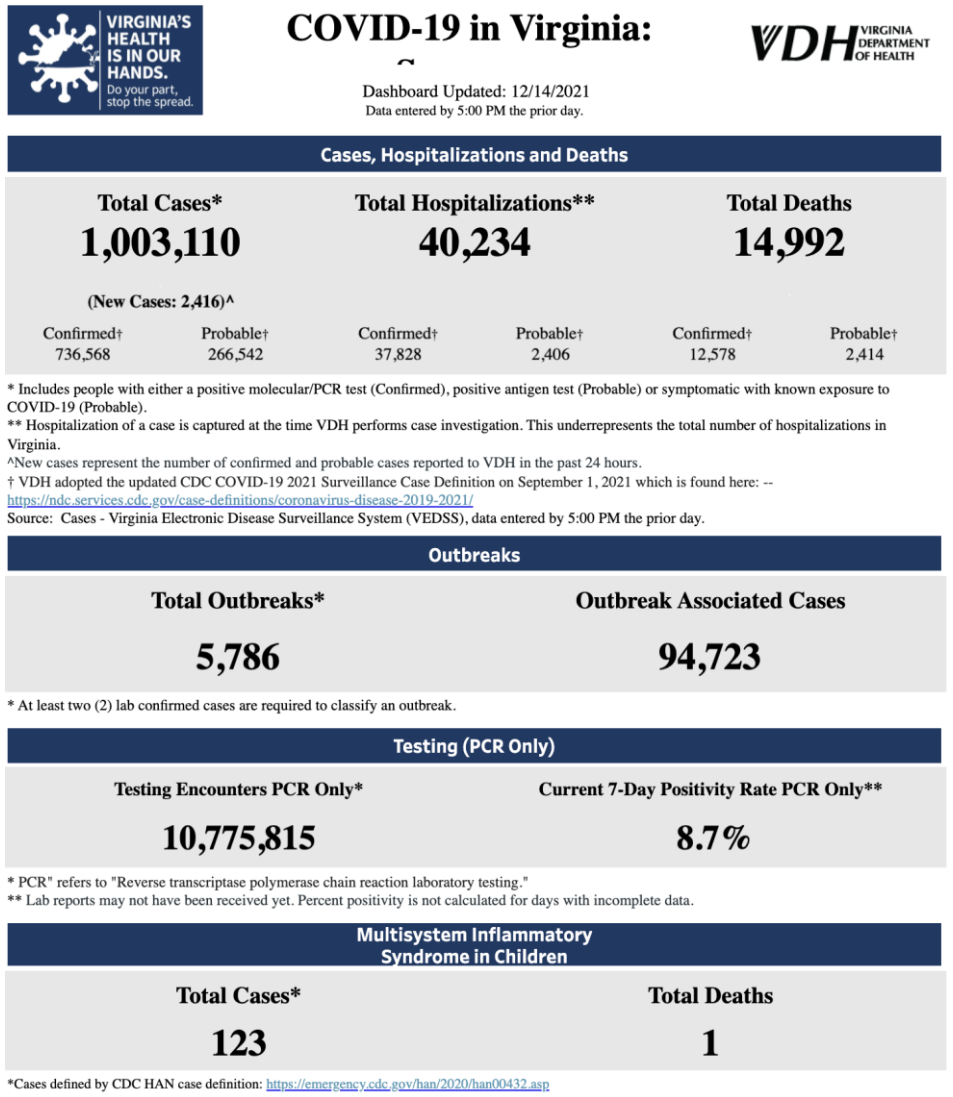
- Thus for 2x there are 2 total infections in the population for every confirmed case recently
- **Case ascertainment is half of that for those with prior immunity**
- Uncertainty design has been shifted to these bounds (previously higher ascertainments as was consistent earlier in the pandemic were being used)



https://covid.cdc.gov/covid-data-tracker/#national-lab

Calibration Approach

- **Data:**
  - County level case counts by date of onset (from VDH)
  - Confirmed cases for model fitting
- **Calibration:** fit model to observed data and ensemble's forecast
  - Tune transmissibility across ranges of:
    - Duration of incubation (5-9 days), infectiousness (3-7 days)
    - Undocumented case rate (1x to 7x) guided by seroprevalence studies
    - Detection delay: exposure to confirmation (4-12 days)
  - Approach captures uncertainty, but allows model to precisely track the full trajectory of the outbreak
- **Project:** future cases and outcomes generated using the collection of fit models run into the future
  - **Mean trend from last 7 days of observed cases and first week of ensemble's forecast used**
  - Outliers removed based on variances in the previous 3 weeks
  - 2 week interpolation to smooth transitions in rapidly changing trajectories
- **Outcomes**: Data driven by shift and ratio that has least error in last month of observations
  - Hospitalizations: 3 days from confirmation, 6.8% of cases hospitalized
  - Deaths: 11 days from confirmation, 1.45% of cases die



VIRGINIA'S HEALTH IS IN OUR HANDS. Do your part, stop the spread.

COVID-19 in Virginia:

VDH VIRGINIA DEPARTMENT OF HEALTH

Dashboard Updated: 12/14/2021
Data entered by 5:00 PM the prior day.

Cases, Hospitalizations and Deaths

Total Cases*	Total Hospitalizations**	Total Deaths
1,003,110	40,234	14,992
(New Cases: 2,416)^		

Confirmed†	Probable†	Confirmed†	Probable†	Confirmed†	Probable†
736,568	266,542	37,828	2,406	12,578	2,414

* Includes people with either a positive molecular/PCR test (Confirmed), positive antigen test (Probable) or symptomatic with known exposure to COVID-19 (Probable).
** Hospitalization of a case is captured at the time VDH performs case investigation. This underrepresents the total number of hospitalizations in Virginia.
^New cases represent the number of confirmed and probable cases reported to VDH in the past 24 hours.
† VDH adopted the updated CDC COVID-19 2021 Surveillance Case Definition on September 1, 2021 which is found here: -- https://ndc.services.cdc.gov/case-definitions/coronavirus-disease-2019-2021/
Source: Cases - Virginia Electronic Disease Surveillance System (VEDSS), data entered by 5:00 PM the prior day.

Outbreaks

Total Outbreaks*	Outbreak Associated Cases
5,786	94,723

* At least two (2) lab confirmed cases are required to classify an outbreak.

Testing (PCR Only)

Testing Encounters PCR Only*	Current 7-Day Positivity Rate PCR Only**
10,775,815	8.7%

* PCR" refers to "Reverse transcriptase polymerase chain reaction laboratory testing."
** Lab reports may not have been received yet. Percent positivity is not calculated for days with incomplete data.

Multisystem Inflammatory Syndrome in Children

Total Cases*	Total Deaths
123	1

*Cases defined by CDC HAN case definition: https://emergency.cdc.gov/han/2020/han00432.asp

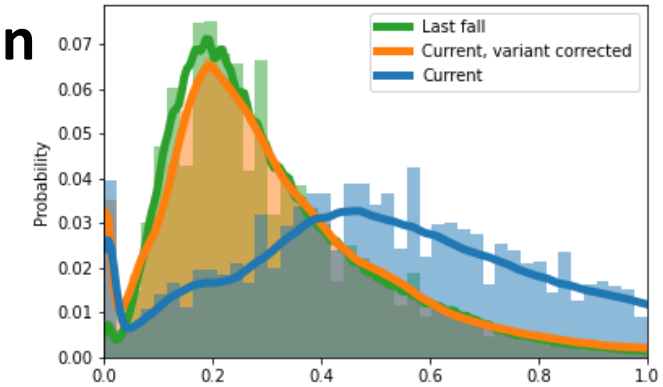
Accessed 8:30am December 15, 2021
https://www.vdh.virginia.gov/coronavirus/

Scenarios – Transmission Conditions

- Variety of factors continue to drive transmission rates
  - Seasonal impact of weather patterns, travel and gatherings, fatigue and premature relaxation of infection control practices
- **Waning Immunity**: Mean of 6 months to a re year protection (rate of 0.0027) similar to Pfizer study
- **Projection Scenarios**:
  - **Adaptive:** Control remains as is currently experienced into the future with assumption that Delta remains as the majority strain
  - **Adaptive-Omicron:** Controls remain the same while the Omicron rapidly dominates prevalence. Has same transmissibility as Delta with 30% immune evasion
  - **Adaptive-FallWinter:** Starting this week the core drivers of transmission from Sept 2020 – Feb 2021 are coarsely replayed but boosted to account for Delta's increased transmissibility
  - **Adaptive-Surge Control:** Starting in one week behaviors and mitigation efforts ramp up over a 2-week period culminating in a 25% reduction in transmission

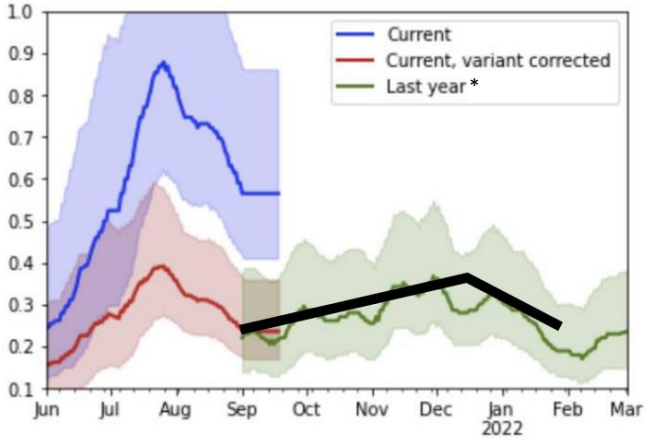
Scenarios – FallWinter Description

September 2020 – February 2021 saw a strong wave of transmission

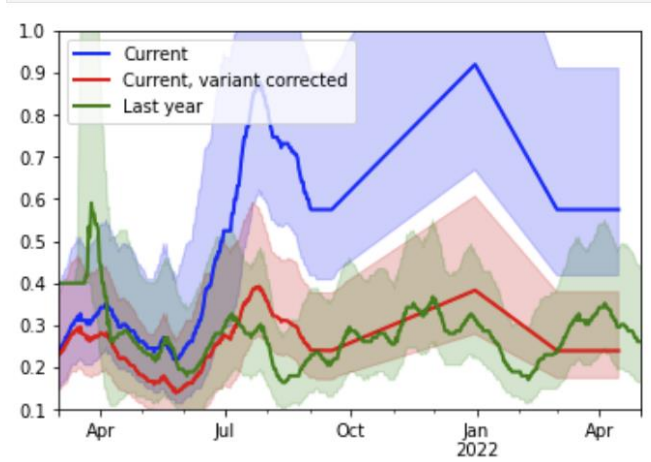


- We analyze previous Fall-Winter's wave vs. current Delta driven wave and observe surprising similarities
  - The distribution of fitted model transmissibility is nearly identical between these periods when corrected for Delta's increased transmissibility
- **FallWinter** tries to capture the "transmission drivers" from the past and use them as if they were to occur again this season but with Delta variant (compared to ancestral)
  - Use the above analysis of fitted model transmissibilities from Sept 2020 – Feb 2021 to guide the future transmissibility from Sept 2021 through Feb 2022, but add the enhanced transmissibility of Delta back in

Fitting:
Black line represents the coarsely fitted base transmissibility



* "Last year" is transplanted into 2021-22



Delta enhanced:
Blue trajectory represents current fitted and then projected transmissibility in FallWinter2020

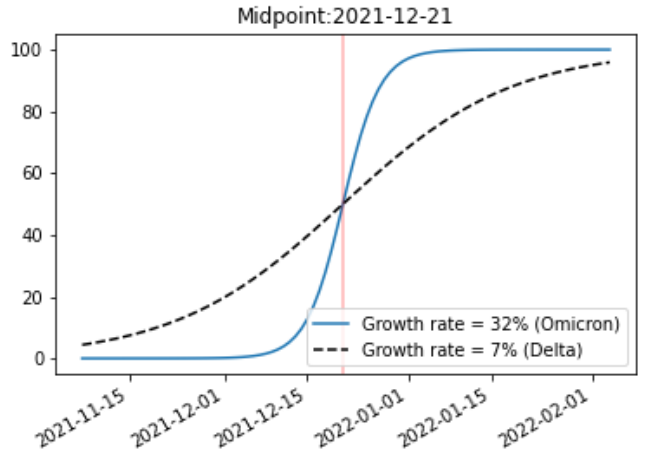
Scenarios – Omicron Description

Omicron shown ability to evade immunity and may be more transmissible

- **Transmissibility**: Evidence exists that it may be more inherently transmissible, for this scenario we conservatively keep Omicron with the **same transmissibility of Delta**
- **Immune Evasion**: Stronger evidence demonstrates that Omicron can cause infection in those with some immunity (natural and vaccine induced). Conservative estimate of **30% immune evasion** allows Omicron to infect 30% of individuals that would have otherwise been protected against Delta
- **Prevalence**: Proportion of cases caused by Omicron variant estimated from growth rates observed in other countries with similar levels of immunity (growth of 32%, doubling in ~3 days)
- **Severity:** Initial reports suggest Omicron may not cause as severe disease as Delta, we use a 50% reduction in severity for hospitalizations and deaths.
  - Recent preprint from South Africa suggests it cold be 70% less, whereas, a PHE report found no evidence of reduced severity.

These are conservative estimates (lower) for both transmissibility and immune evasion, even so growth is stronger than previously observed

Estimated Prevalence curve for US



Predominance occurs before Jan 1, 2022

Scenarios – Vaccination Conditions

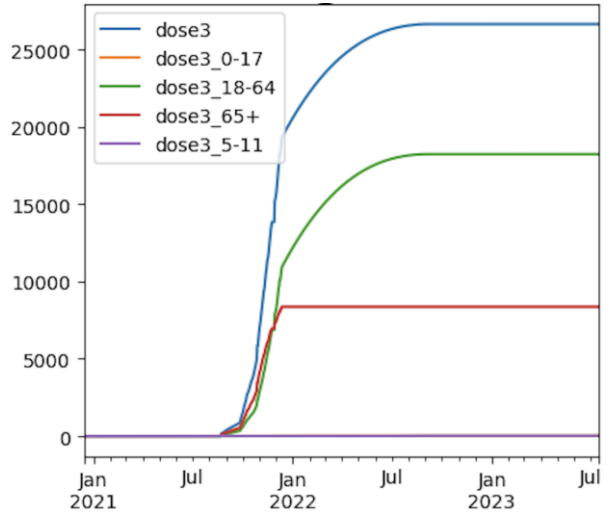
Vaccine Characteristics

- **Pfizer/Moderna**: 50% after first dose, 95% after second dose (3.5 week gap) **J & J** : 67% efficacy after first dose
- Delay to efficacy from doses is 14 days, immunity lasts at least 7m (NEJM study)

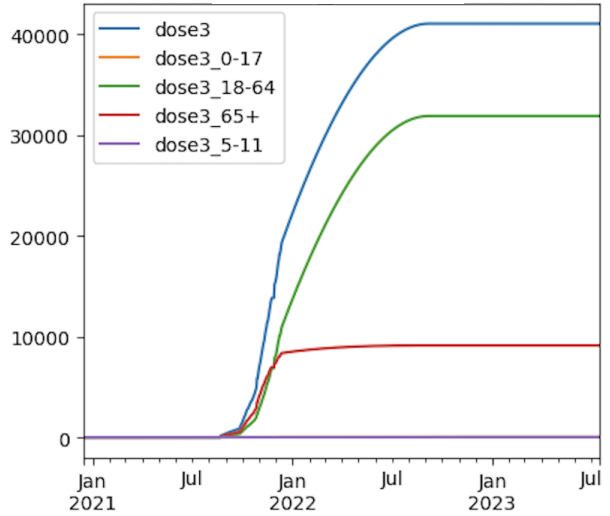
Vaccine Administration Scenarios

- **Status quo (no label):**
  - **Eventual coverage**: COVIDcast corrected acceptance estimates (statewide mean is ~80% adults, 65% of population) reached by end of January.
  - **Children (5-11):** Follow rates of 12-16 year olds, max out at 80% of adult acceptance
  - **3rd doses:** Top out with total coverage of 40%
- **Optimistically High Boosting (HighBoost):**
  - **Eventual coverage**: COVIDcast corrected acceptance estimates (statewide mean is ~80% adults, 65% of population) reached by end of January.
  - **Children (5-11):** Follow rates of 12-16 year olds, max out at 80% of adult acceptance
  - **3rd doses:** Top out with total coverage of 70%
- Acceptance at county level = regional acceptance +/- relative current vax
- Front-loaded rollout (two-thirds of the remaining in half the time)

Status Quo



High Boost



Projection Scenarios – Combined Conditions

Name	Txm Controls	Vax	Description
Adaptive	C	SQ	Likely trajectory based on conditions remaining similar to the current experience
Adaptive-HighBoost	C	VO	Vaccination through January 2022 reaches an optimistically high level of expanded coverage (85%)
Adaptive-Omicron	C	SQ	Assumes rapid dominance of immune evading variant. Conservatively uses no transmission advantage to Delta but 30% of previously immune individuals are susceptible to infection from Omicron
Adaptive-SurgeControl	25%	SQ	Transmission rates in the next month reduced through increased control from non-pharmaceutical interventions, with status quo vax and Delta
Adaptive-FallWinter	FallWinter	SQ	Transmission rates coarsely follow the rates from last September through this February but are boosted by Delta's enhanced transmissibility

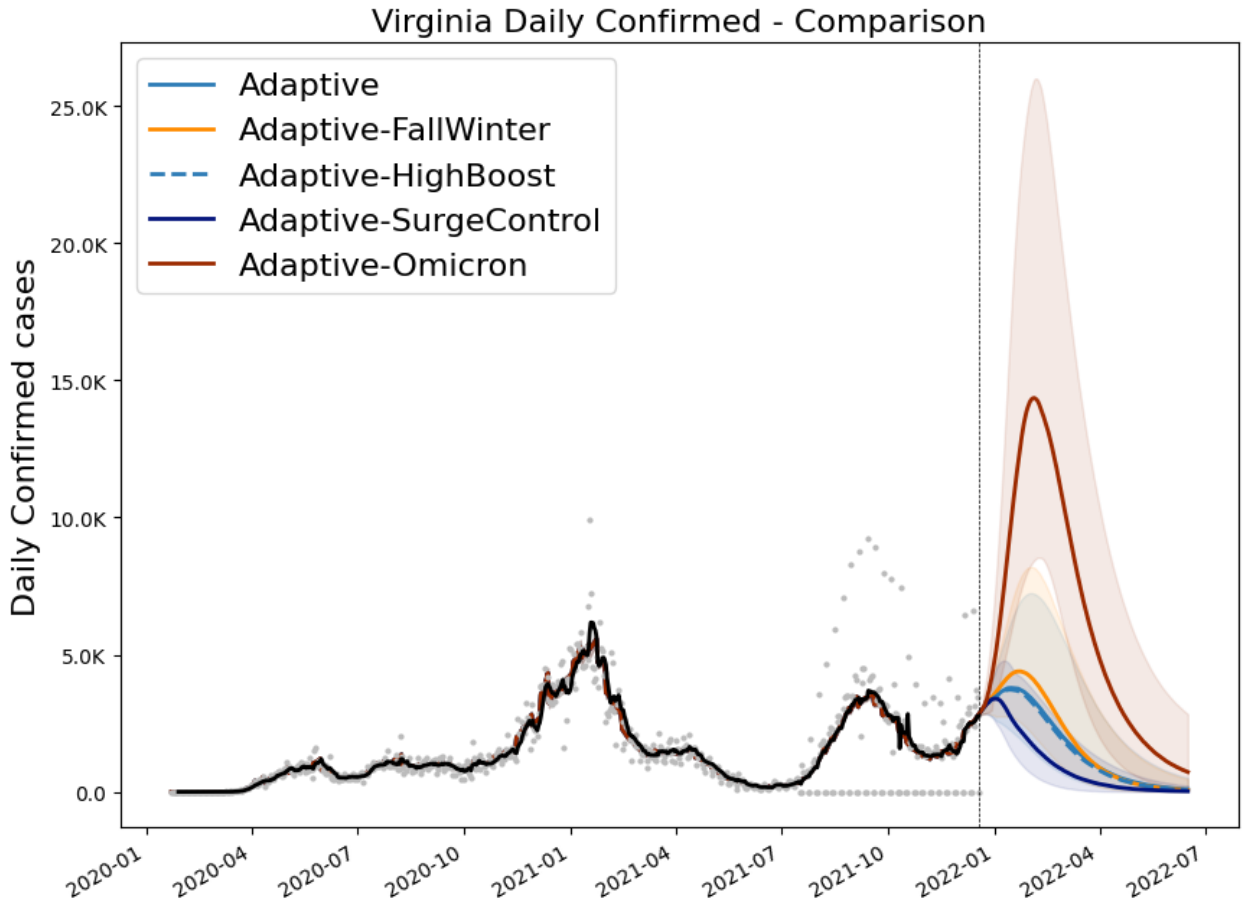
Transmission Controls:
C = Current levels persist into the future
25% = Transmission rates are reduced by 25% with a gradual introduction, concluding in 4 weeks
FallWinter2020 = Transmission rates from Sept 2020 – Feb 2021 are coarsely replayed but boosted by Delta's increased transmissibility

Vaccinations:
SQ = Status quo acceptance leads to low rates of vaccination through the summer
VO = Vaccination acceptance optimistically expands with increased rates through the summer

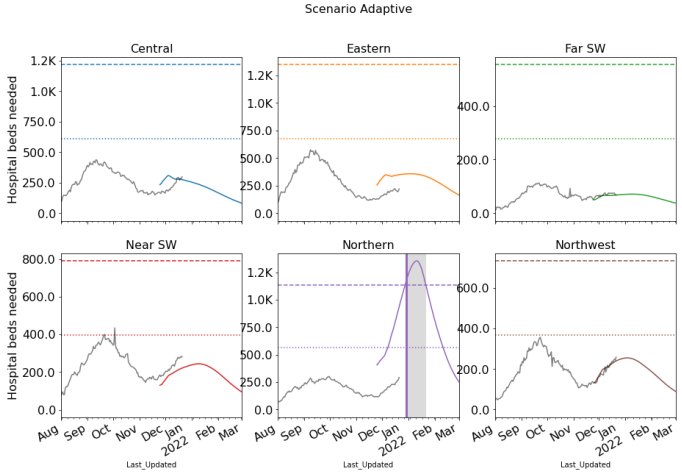
Model Results

Outcome Projections

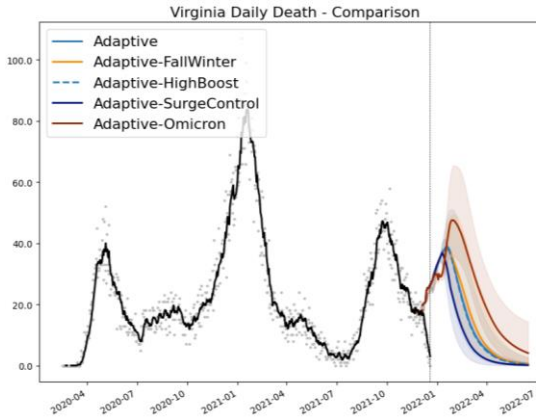
Confirmed cases



Estimated Hospital Occupancy

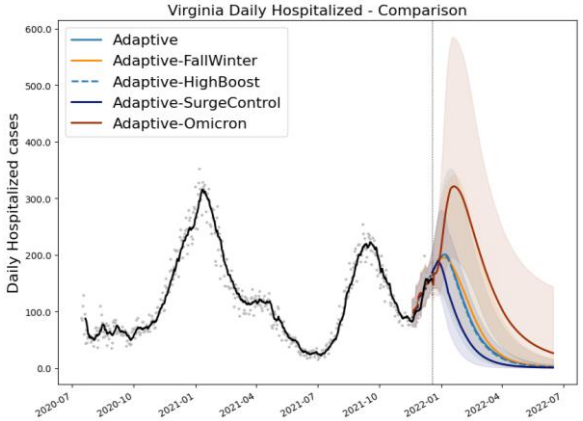


Daily Deaths



Death ground truth from VDH "Event Date" data, most recent dates are not complete

Daily Hospitalized



Hospitalization is slightly miscalibrated this week, seems to be driven by Northern region. Trends should be correct but absolute numbers are misaligned

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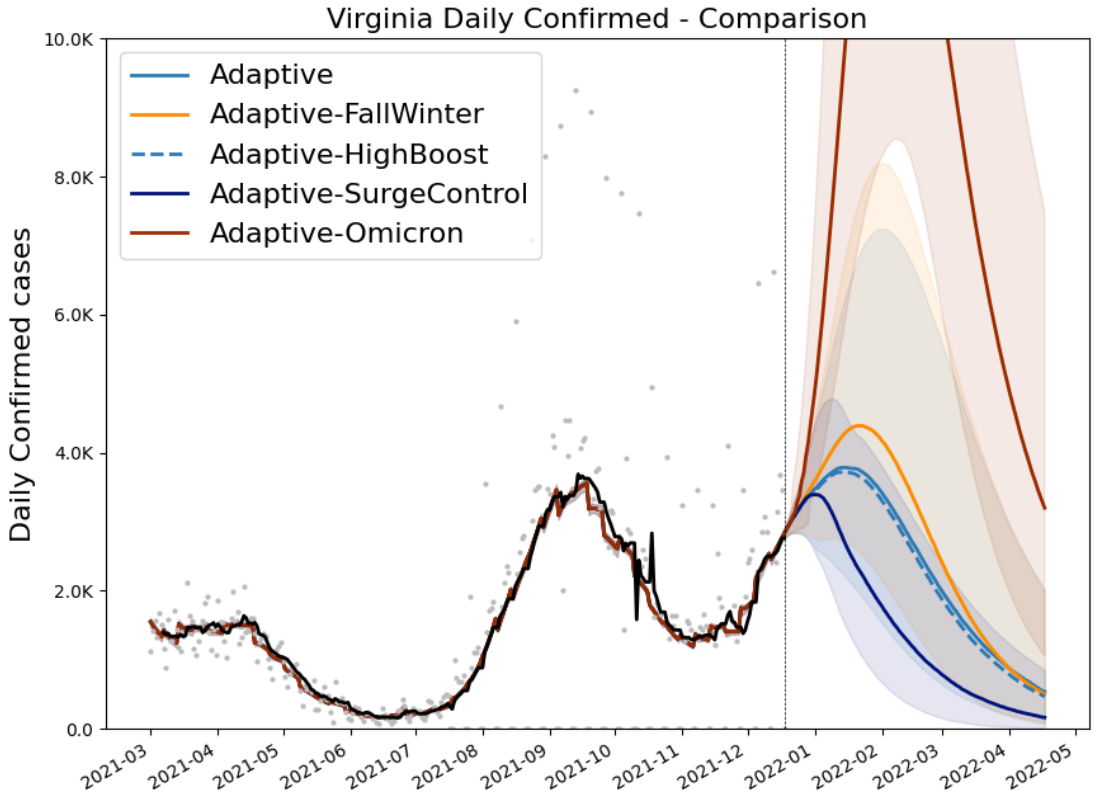
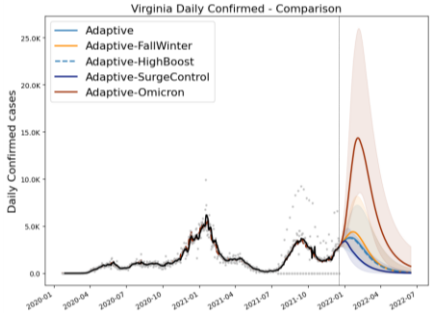
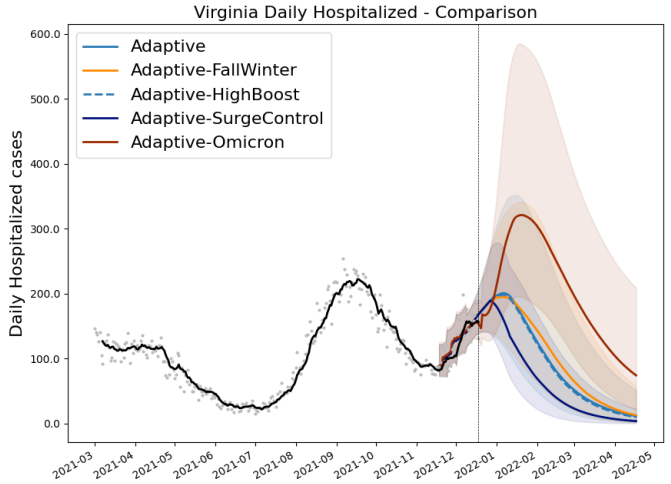
Outcome Projections – Closer Look

Confirmed cases

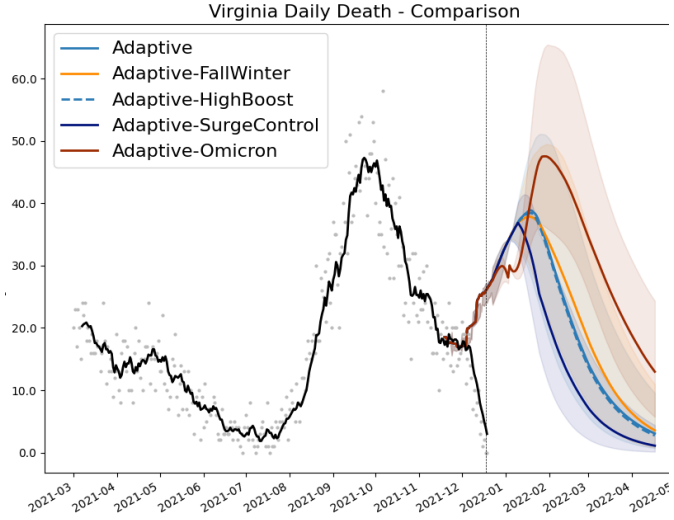




Daily Hospitalized



Daily Deaths



Death ground truth from VDH "Event Date" data, most recent dates are not complete

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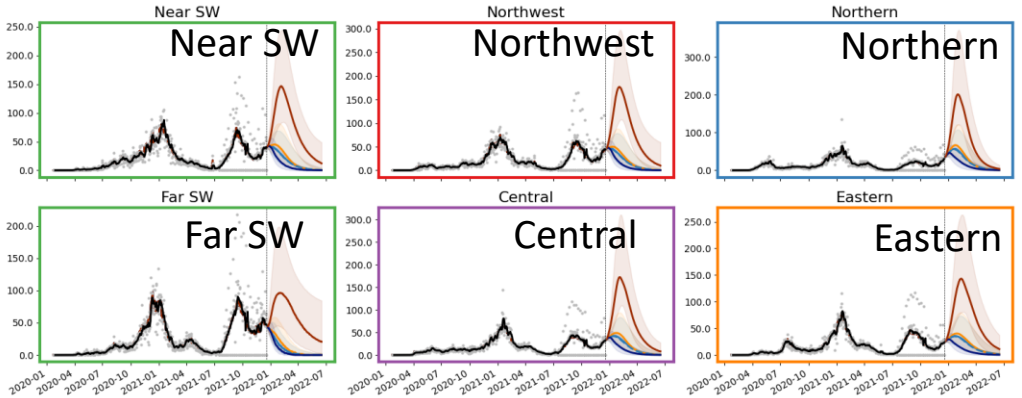
Detailed Projections: All Scenarios

Projections by Region

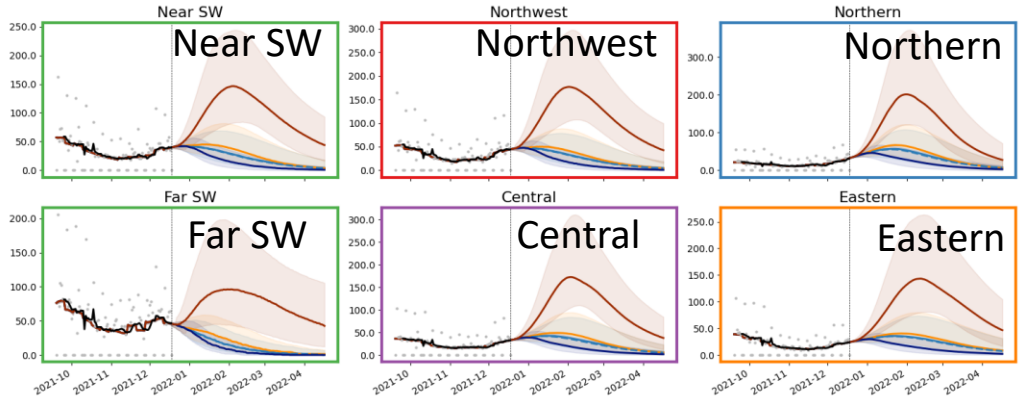


Projections by District

Daily confirmed cases) by rate (per 100K) District (grey with 7-day average in black) with simulation colored by scenario

Detailed Projections: All Scenarios - Closer Look

Projections by Region



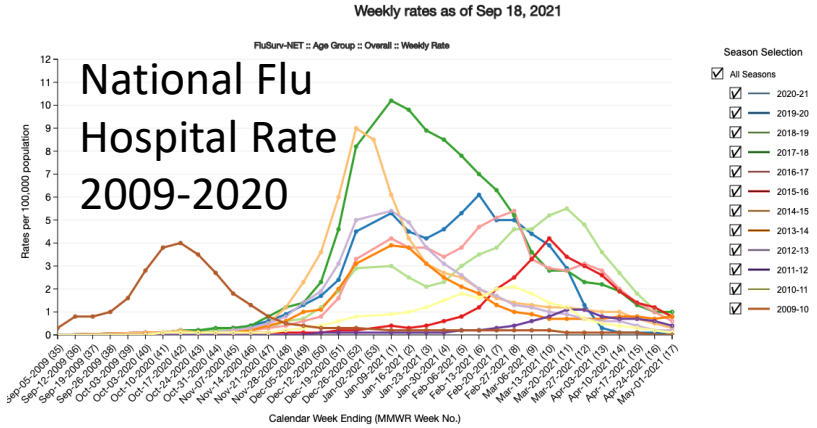
Projections by District

Daily confirmed cases by rate (per 100K) District (grey with 7-day average in black) with simulation colored by scenario

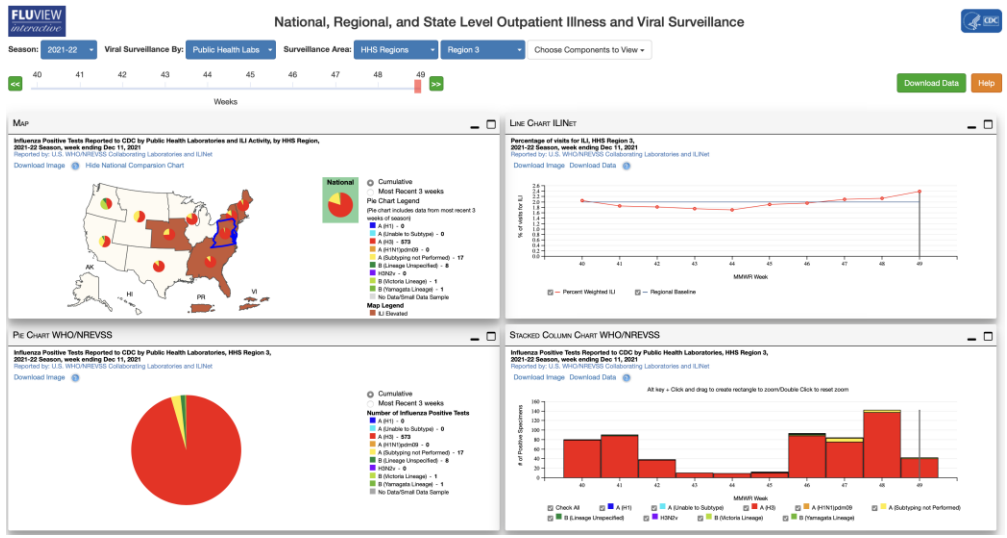
Impact of Influenza based on Previous Intense Flu Seasons

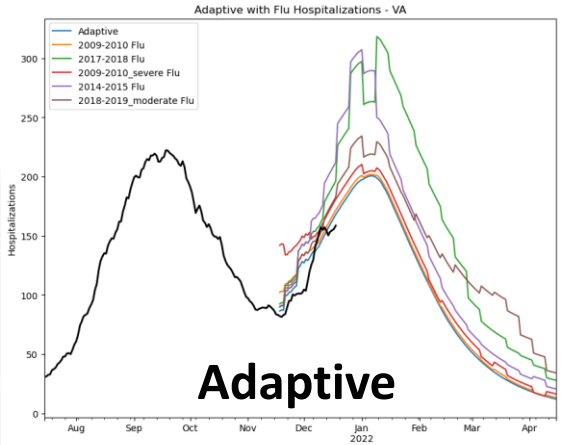
Augment COVID-19 daily hospitalizations with that of past Influenza seasons

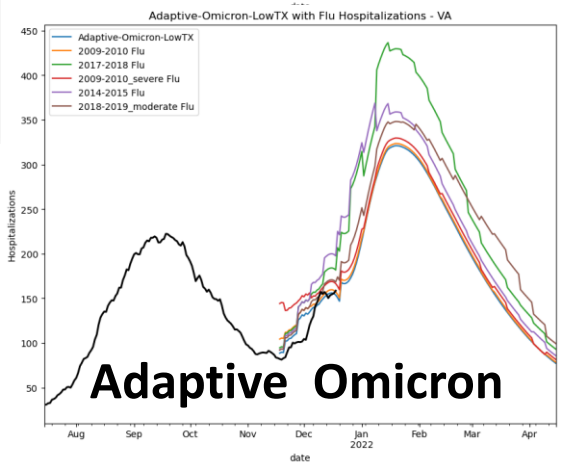
- Include hybrid seasons that use timing of one season but are scaled by severity of another
- Due to limited historical data on Virginia flu hospitalizations currently using national rates applied to VA population



https://gis.cdc.gov/GRASP/Fluview/FluHospRates.html







2009-10 – Pandemic 2009 H1N1 season

2017-18 – Timing and severity of 2017-18 season

2009-10_severe – Timing of 2009 pandemic (early) with the severity of the 2017-18 season

2014-15 – Timing and severity of 2014-15 season

2018-19_moderate – Timing of 2018-19 (late) season with severity of 2014-15

Influenza A activity up in our region
Labs show high levels of H3 this season
(Influenza A H3N2 is more severe)

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Key Takeaways

Projecting future cases precisely is impossible and unnecessary.
Even without perfect projections, we can confidently draw conclusions:

- **Case rates grew after holiday break but growth has slowed slightly, keeping case rates high as the anticipated arrival of Omicron may fuel more rapid growth in the near term**
- VA 7-day mean daily case rate up to 30/100K from 26/100K; US is up to 36/100K (from 35/100K)
- Projections show a continued rise of cases which becomes more extreme under Omicron and FallWinter scenarios that anticipate likely drivers of future transmission
- Recent updates:
  - Overhauled model structure further refined to better capture different tiers of immunity and the immune evasion of the Omicron variant
  - Analysis of the effects of increasing 3rd dose coverage

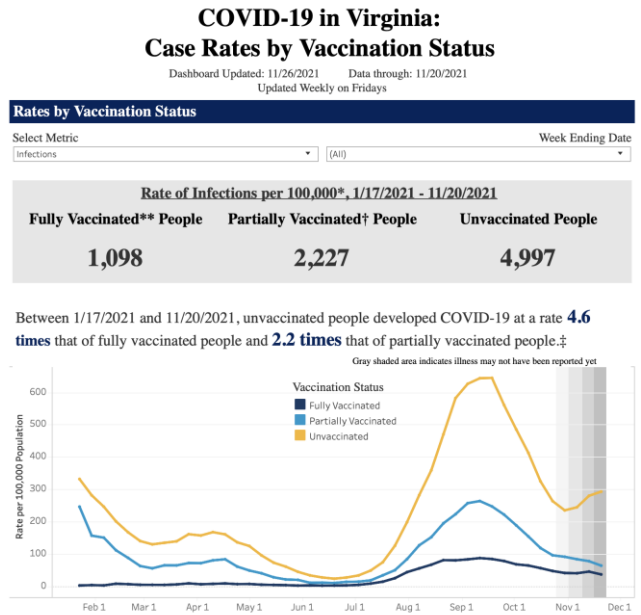
The situation continues to change. Models continue to be updated regularly.

Additional Analyses

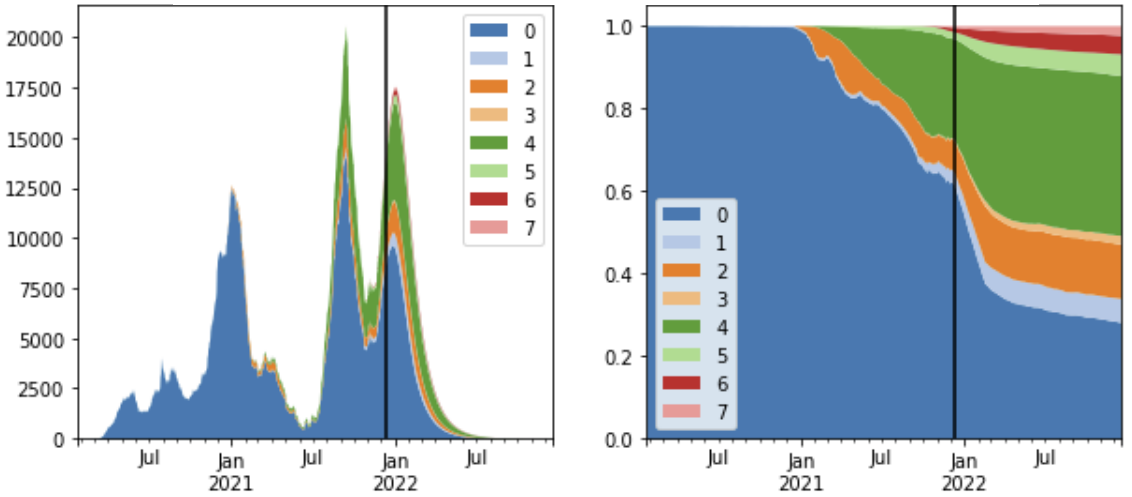
New Infections by Vaccine Status

Infections among Naïve, Vaccinated, and Partial Vaccinated

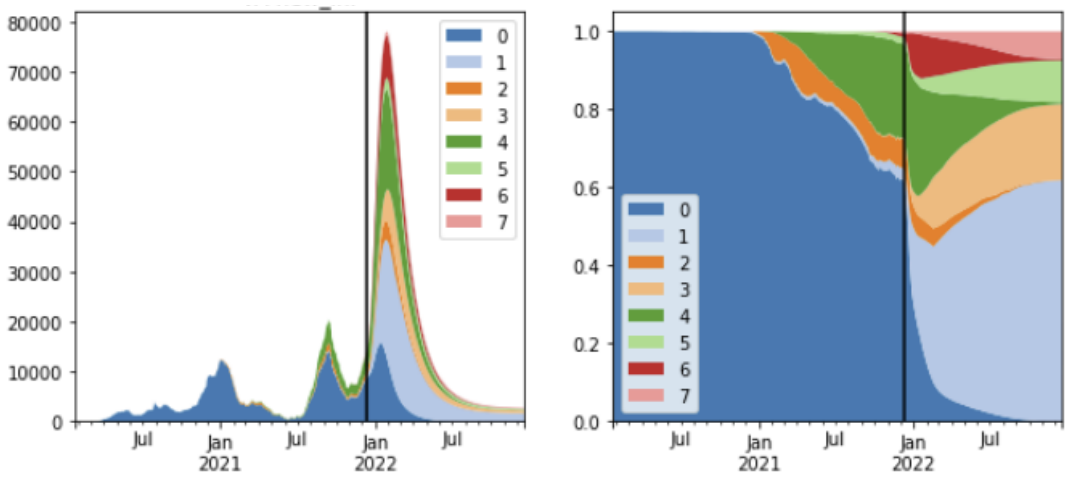
- VDH data for cases with known vaccination status show ~20-30% of current infections come from tiers with some vaccine induced immunity (~20% full and 5-10% partial)
- Model estimates of all infections are similar however, under the Omicron scenario the vast majority of future cases will be from those with prior immunity (due immune evasion)
- Infections in those with prior immunity are likely to be less severe (less hospitalizations and deaths)



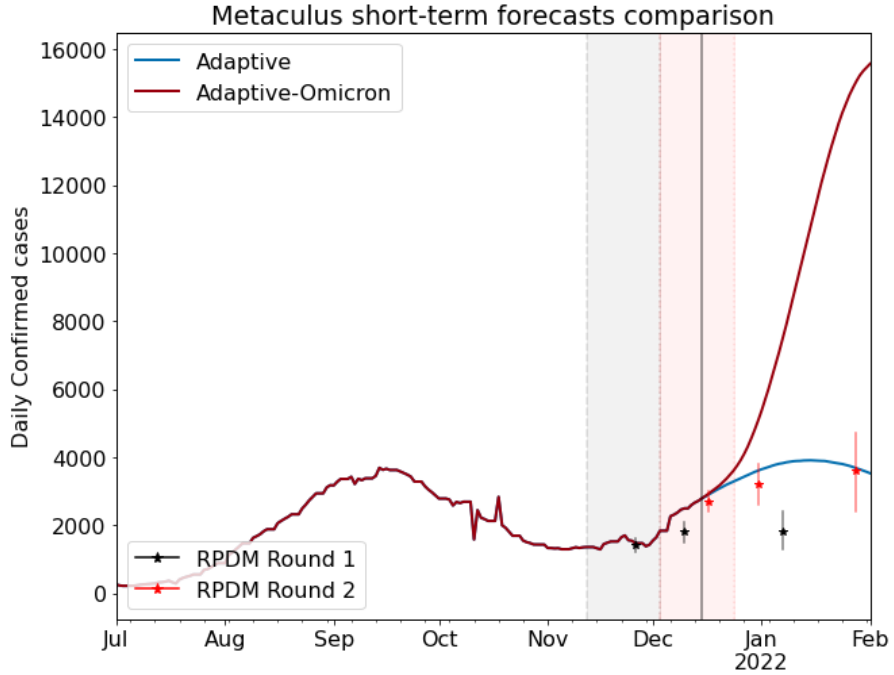
Adaptive - New Infections by Immune Tier



Adaptive-Omicron New Infections by Immune Tier



Metaculus - Short Term & Omicron Forecasts

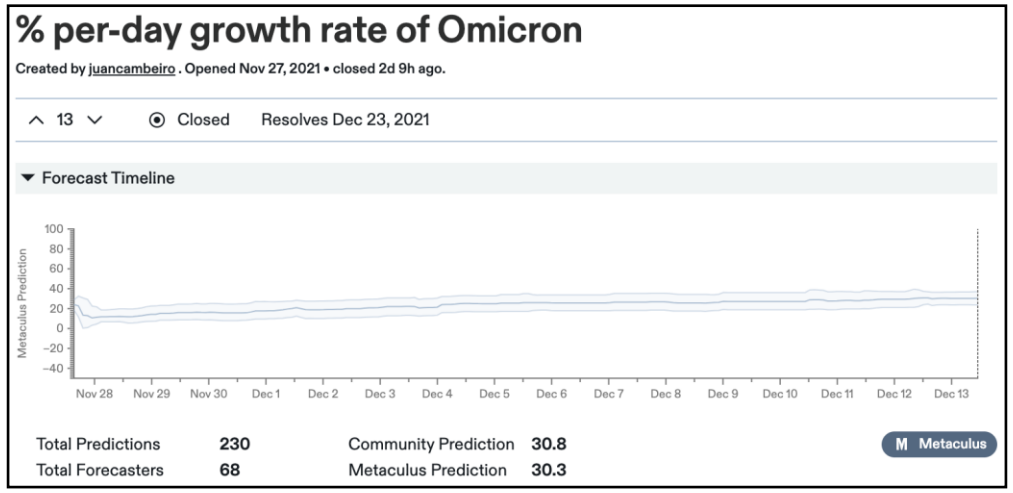


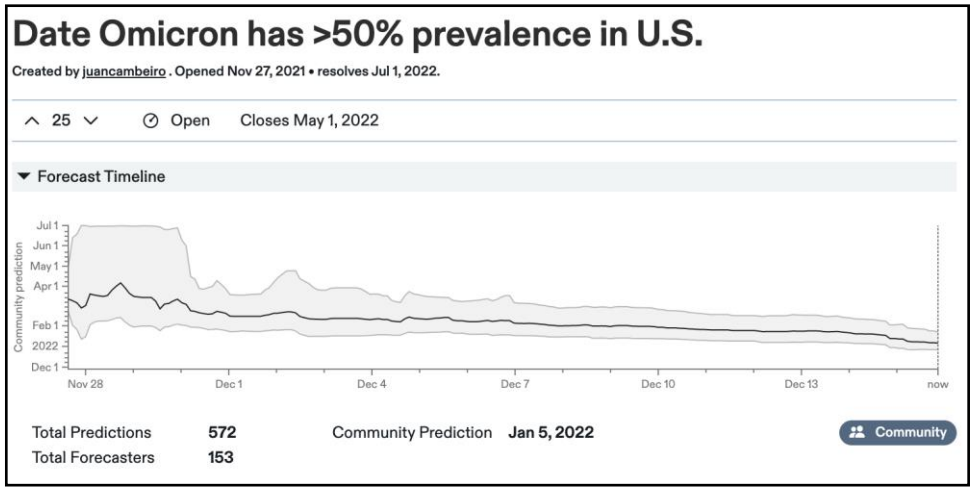
Short-term[1]

- Round 1 forecasts underpredicted current surge
- Round 2 forecasts are more similar to current Adaptive, but much lower than Omicron scenario

Omicron[2]

- Community estimate of growth rate is similar to current model input **(~31%)**
- Predicted midpoint for US **(January 5th, 2022)** is later (and trending downwards from early prediction)





1 https://www.metaculus.com/tournament/realtimepandemic/
2 https://www.metaculus.com/questions/8759/forecasting-coronavirus-variant-omicron/

Overview of relevant on-going studies

Other projects coordinated with CDC and VDH:

- **Scenario Modeling Hub:** Consortium of academic teams coordinated via MIDAS / CDC to that provides regular national projections based on timely scenarios
- **Genomic Surveillance:** Analyses of genomic sequencing data, VA surveillance data, and collaboration with VA DCLS to identify sample sizes needed to detect and track outbreaks driven by introduction of new variants etc.
- **Mobility Data driven Mobile Vaccine Clinic Site Selection:** Collaboration with VDH state and local, Stanford, and SafeGraph to leverage anonymized cell data to help identify

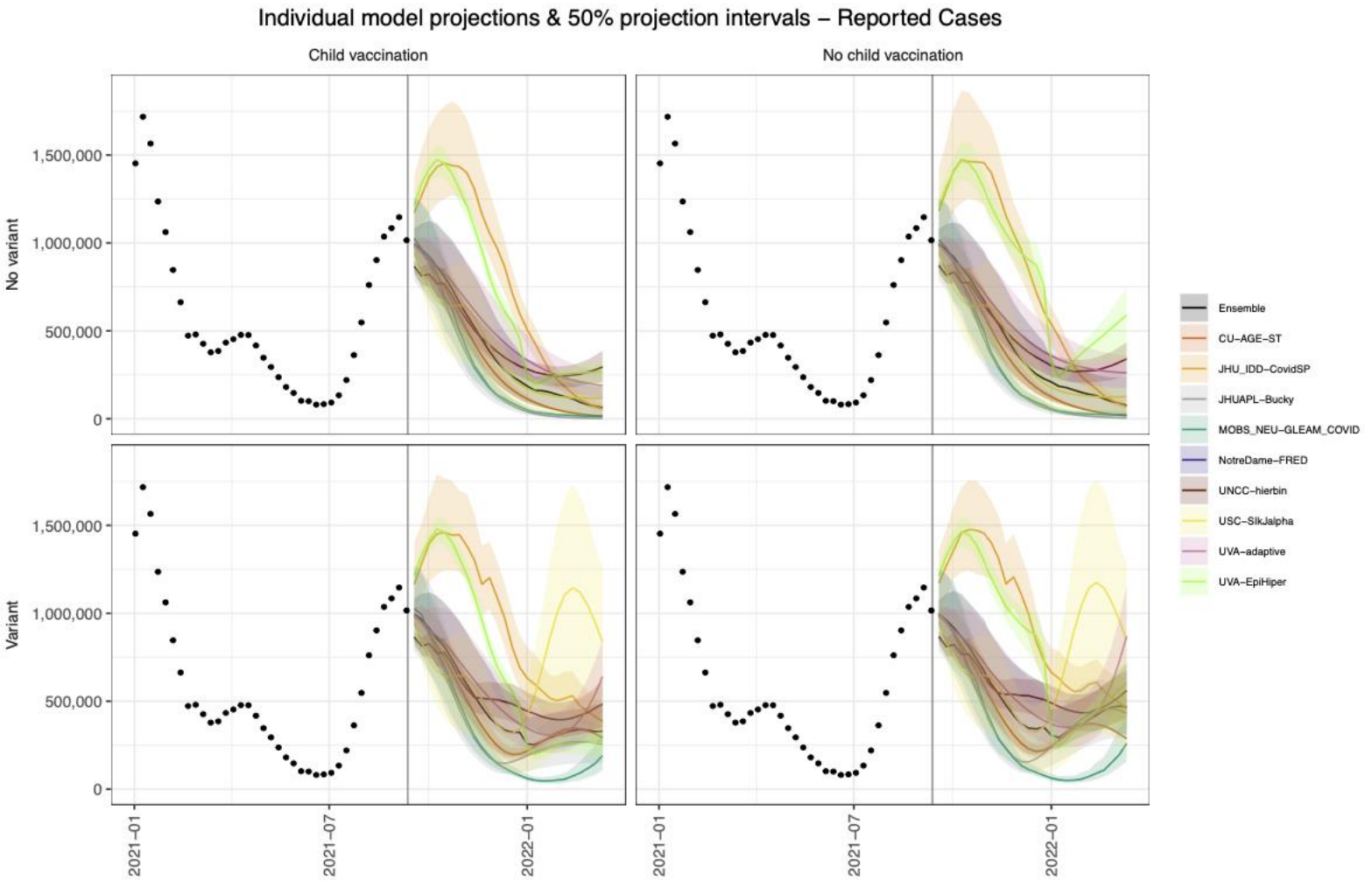
COVID-19 Scenario Modeling Hub

Collaboration of multiple academic teams to provide national and state-by-state level projections for 4 aligned scenarios that vary vaccine rates (high – low) and impact of the Delta variant (high and low)

- Round 9 released to assist in support of 5-11 vax consideration (ACIP meeting Sept 22-23)
- Rounds 4-8 now available

Round 4 Results were published May 5th, 2021 in MMWR

https://covid19scenariomodelinghub.org/viz.html



COVID-19 Scenario Modeling Hub – Round 7

Round 7 scenarios explore the effects of a variant similar to Delta (B.1.617.2) against different backgrounds of vaccination. Includes some vax escape

Vaccinations in 5-11 start in Nov

- Follows same rates as adolescents

Emerging Variant Impact (5% prevalence on Nov 15)

- 50% boost as it eventually predominates

We consider a 2x2 scenario design, where childhood vaccination (5-11 years) is on the first axis, and a change in virus transmissibility is on the second axis. The second axis reflects a stress test, illustrating the potential impact of a new variant arising during the projection period:

	The same mix of variants circulate throughout the projection period. No change in virus transmissibility.	A more transmissible variant emerges, comprising 1% of circulating viruses on **Nov 15**. The new variant is **1.5X** as transmissible as viruses circulating at the beginning of the projection period.
Vaccination among 5-11yrs is approved and immunization begins on Nov 1. Each state's uptake rate reflects the percent coverage increases observed for 12-17-year-olds since distribution began on May 13.	A	C
No vaccination for children under 12	B	D

https://covid19scenariomodelinghub.org/viz.html

Preliminary Analysis of Impact of Waning and 3rd doses

Study to assess impact of waning rate and 3rd dose coverage levels

Waning rate: Duration population remains in an immune state (Vax or Recovered) until becoming susceptible

- Pessimistic: Mean duration 6 months
- Optimistic: Mean duration 1 year

3rd Dose Coverage: Proportion of Fully Vaccinated that receive a 3rd dose and return to full protection

- High: 70% coverage
- Low: 40% coverage

Scenario	Waning Rate	3rd Dose Coverage
A: optWan_highBoo	1 year	70%
B: optWan_lowBoo	1 year	40%
C: pessWan_highBoo	6 months	70%
D: pessWan_lowBoo	6 months	40%

Partial Protection for:

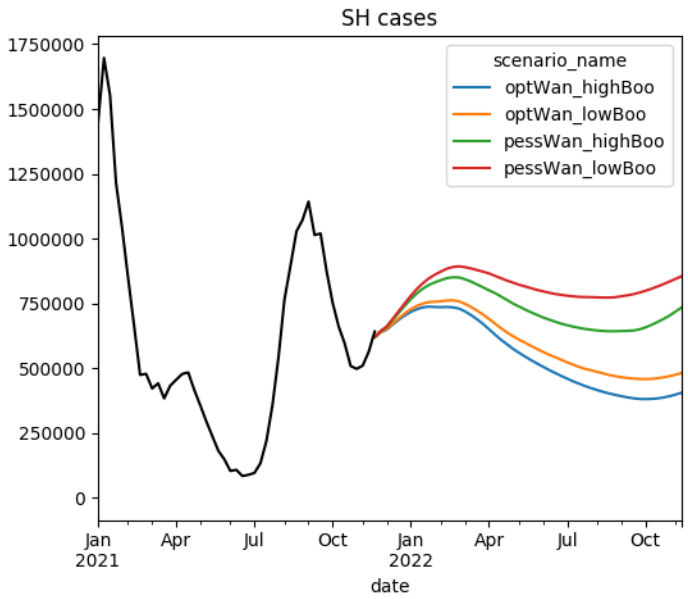
Optimistic Waning

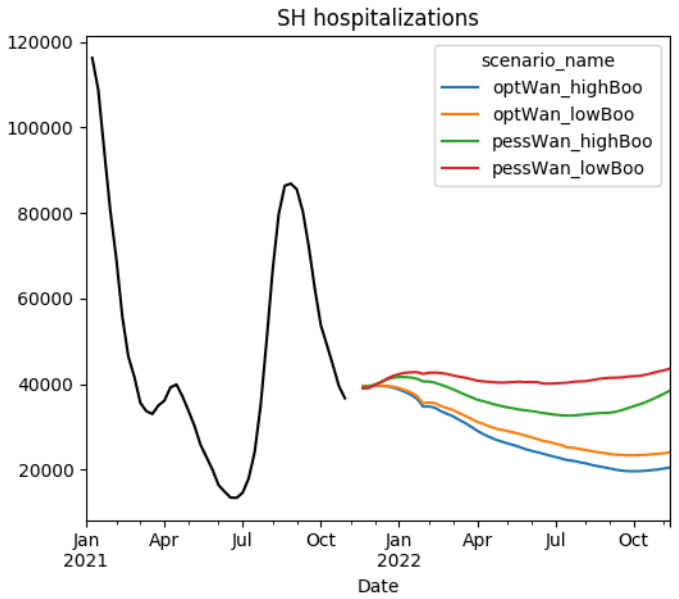
Protection against	Less than 65	65 +
Infection	60%	40%
Hospitalization	90%	80%
Death	95%	90%

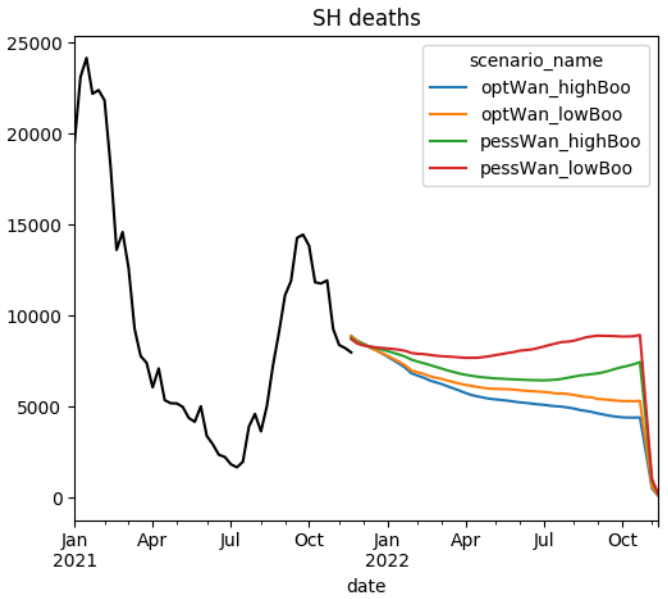
Pessimistic Waning

Protection against	Less than 65	65 +
Infection	50%	30%
Hospitalization	80%	70%
Death	90%	85%

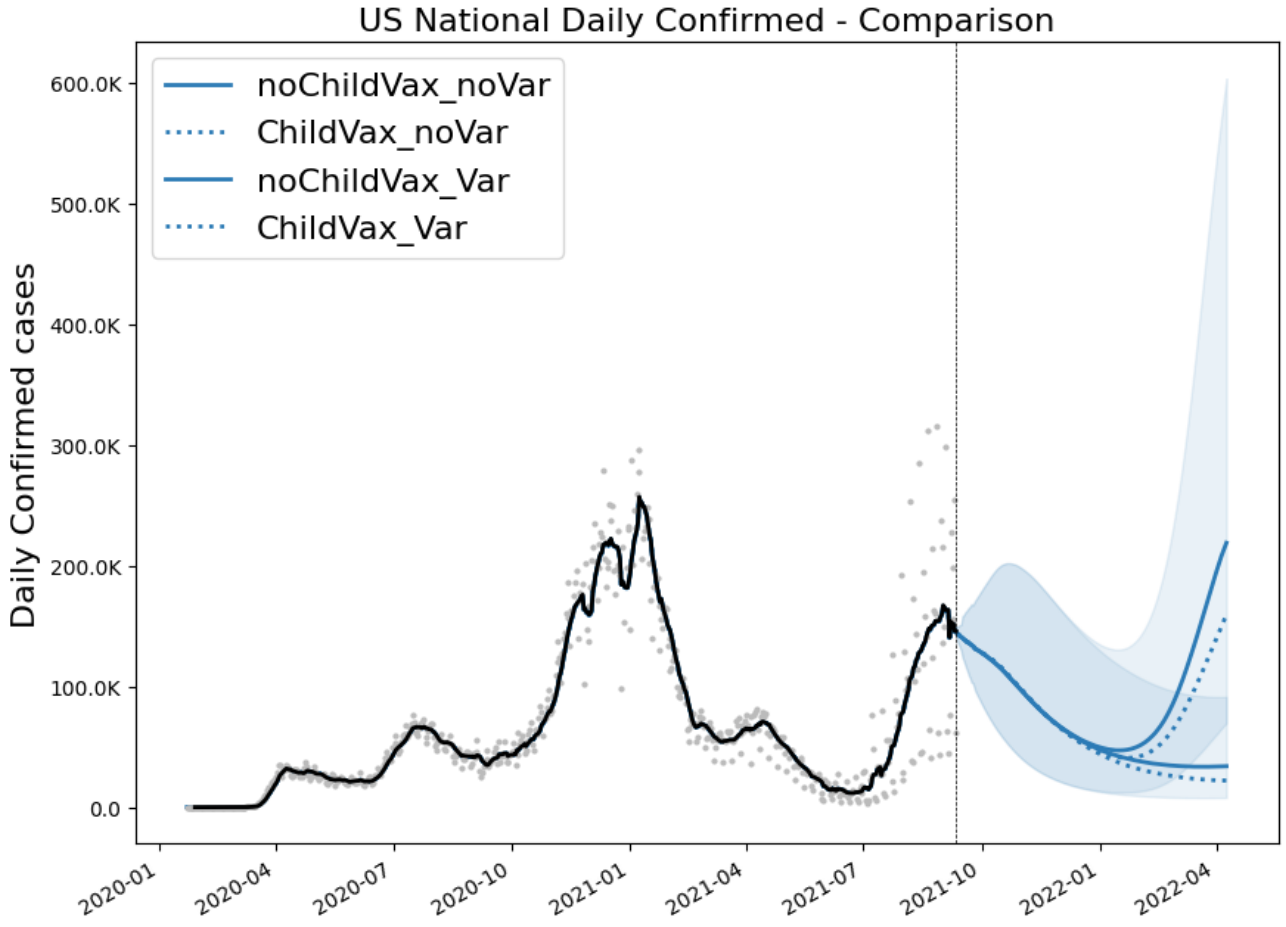
Preliminary Analysis of Impact of Waning and Boosters

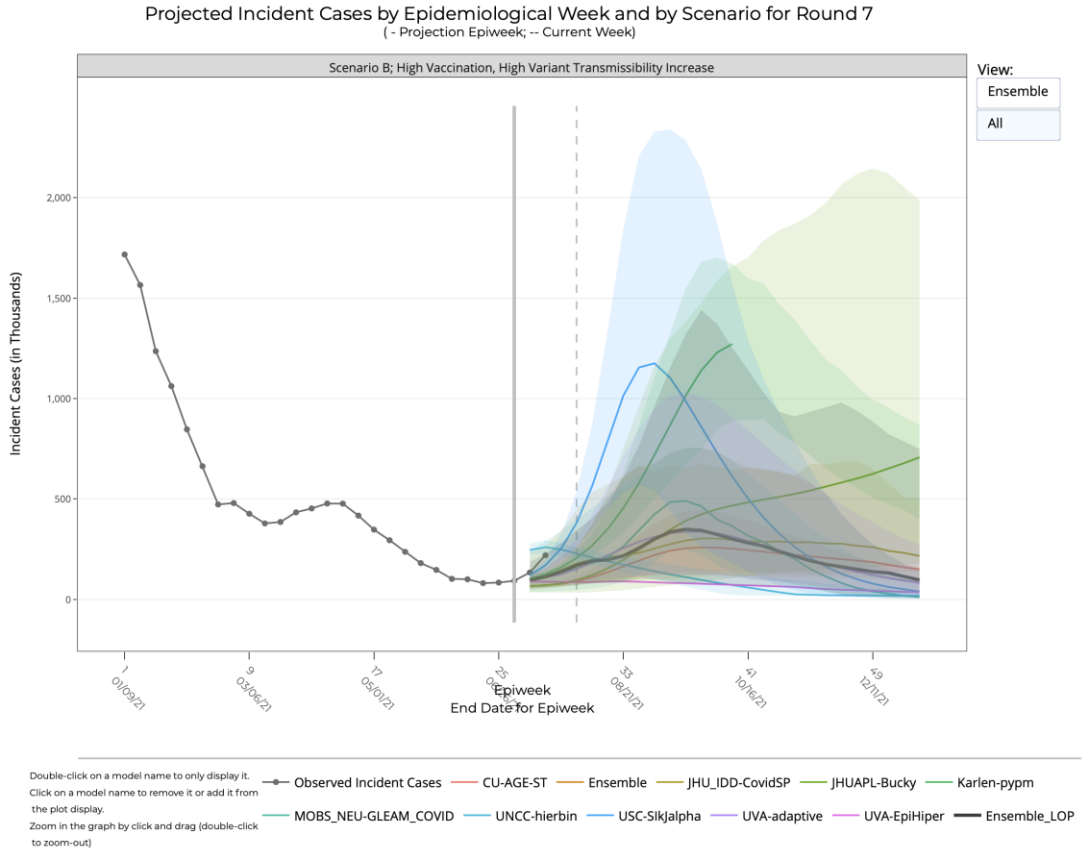






Modeling Hub – Round 9 Prelim Results

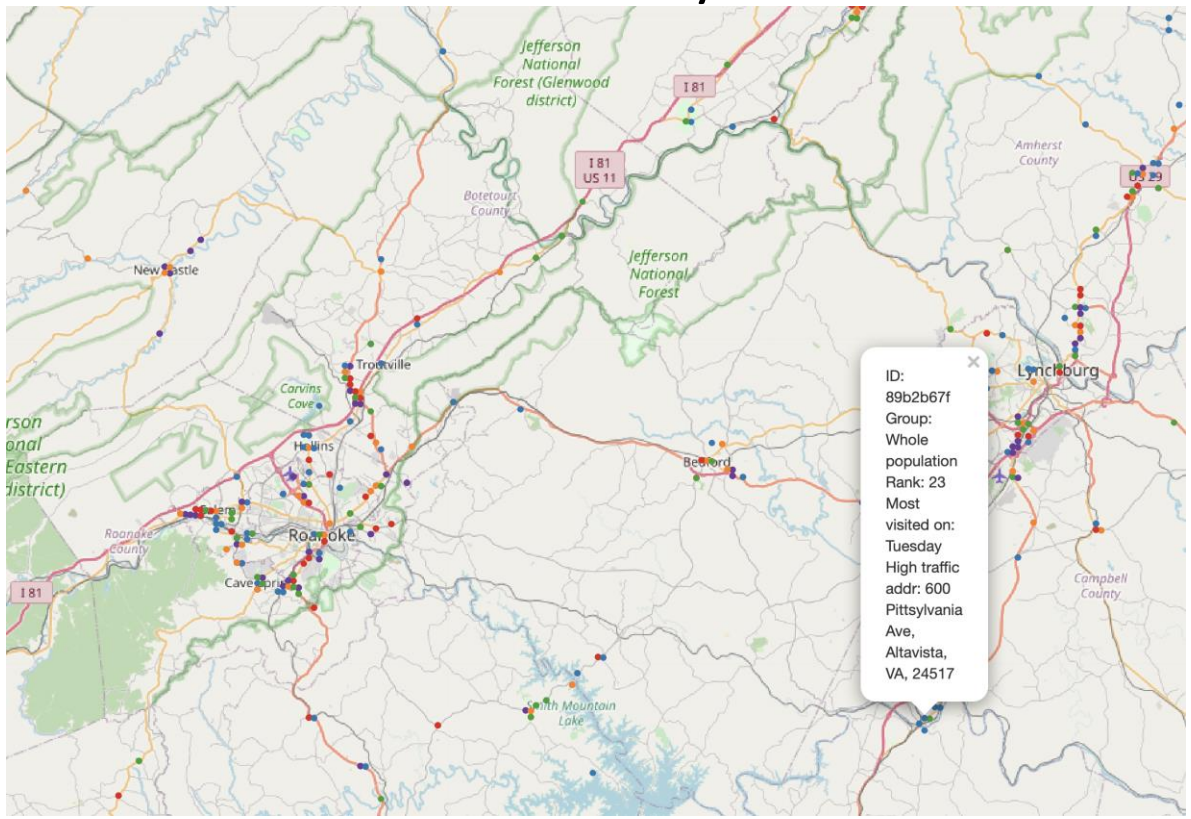




https://covid19scenariomodelinghub.org/viz.html

Data Recommended Mobile Vax Clinic Sites

Detailed and Timely Locations



Data Delivered and Disseminated to Locals

Provides a list of areas most visited by a given demographic group based on SafeGraph mobility data that links visits to specific sites and the home Census Block Group of the anonymized visitors

Demographic Groups: Black, Lantinx, Young Adults (20-40), Unvaccinated, and Whole Population

Data Included: Rank, Weight, most visited Day of Week, Highly Visited Address, and Lat-Long of area

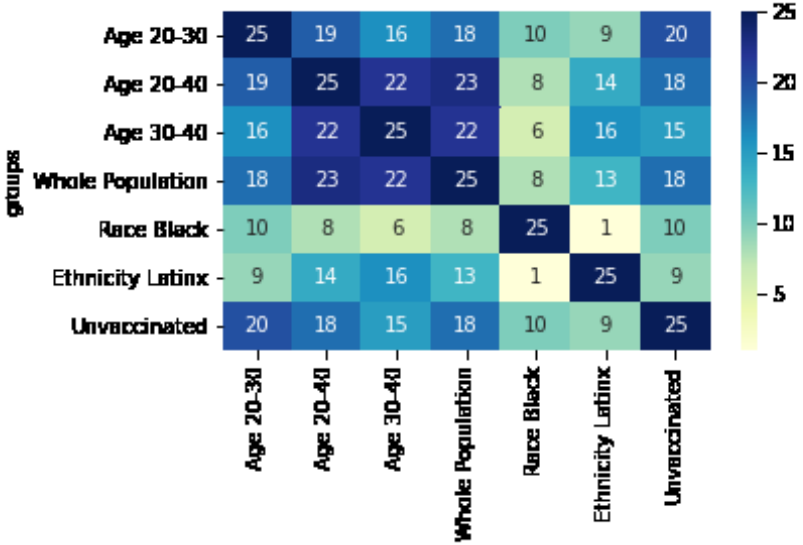
Goal: Provide frequently visited locations based on populations and vaccination levels one desires to reach

Example: List of location in the Southside frequented by 20-40 year olds

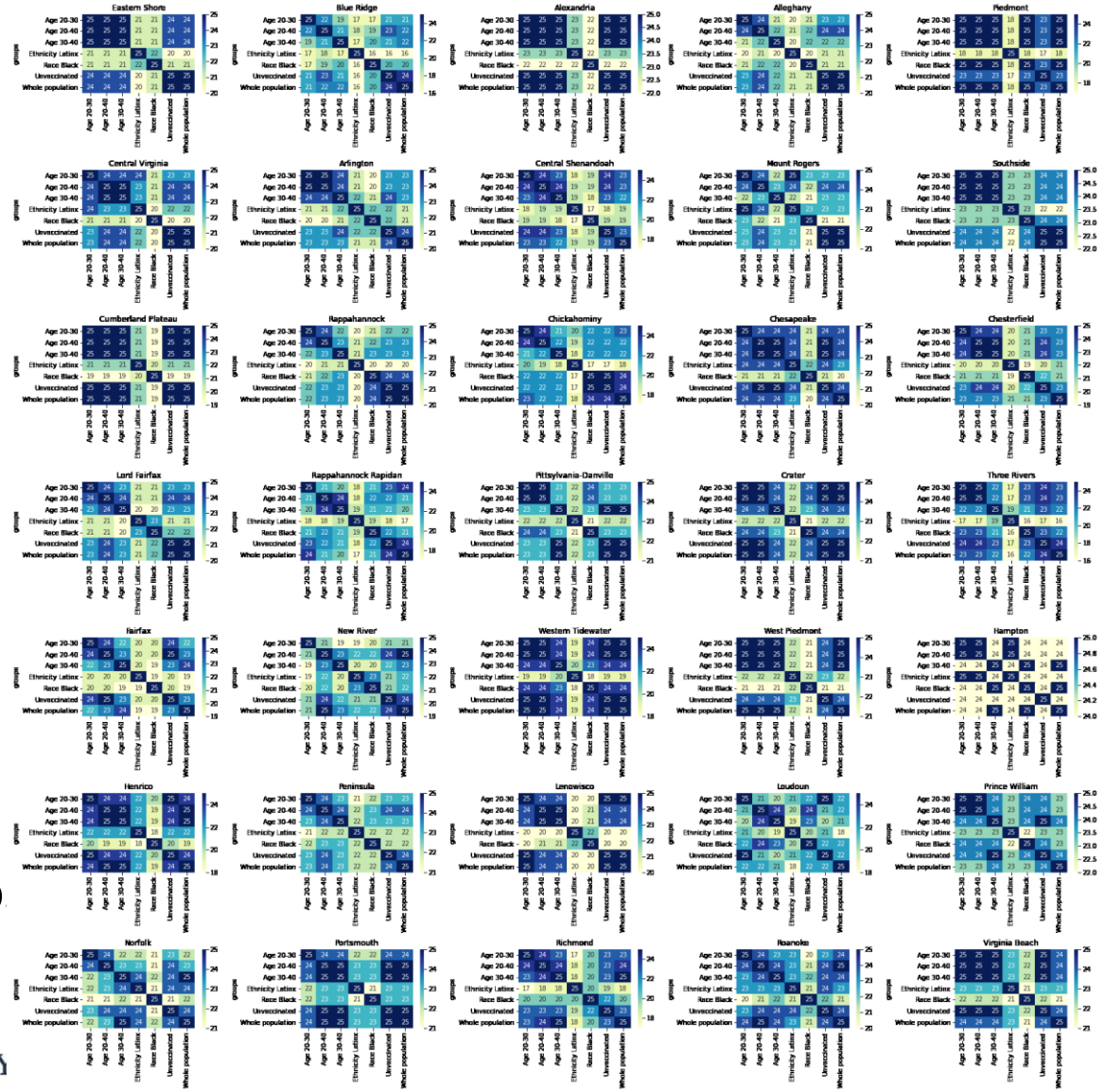
Data Recommended Mobile Vax Clinic Sites

Overlap of locations between groups

State Level



Within VDH Health Districts



Different groups visit different areas

- Least overlap between Black and Latinx
- Overlap in ages highest, but drops with large gap
- Districts have different overlap patterns

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References

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Biocomplexity Institute. COVID-19 Surveillance Dashboard. https://nssac.bii.virginia.edu/covid-19/dashboard/

Google. COVID-19 community mobility reports. https://www.google.com/covid19/mobility/

Biocomplexity page for data and other resources related to COVID-19: https://covid19.biocomplexity.virginia.edu/

Questions?

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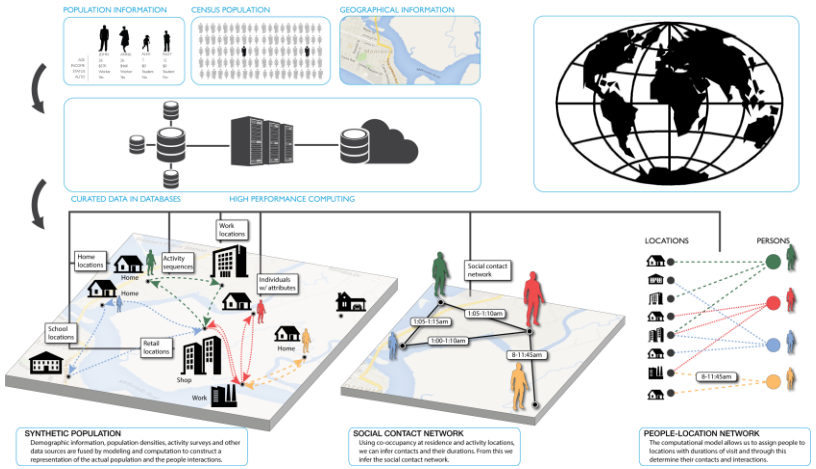
Supplemental Slides

Agent-based Model (ABM)

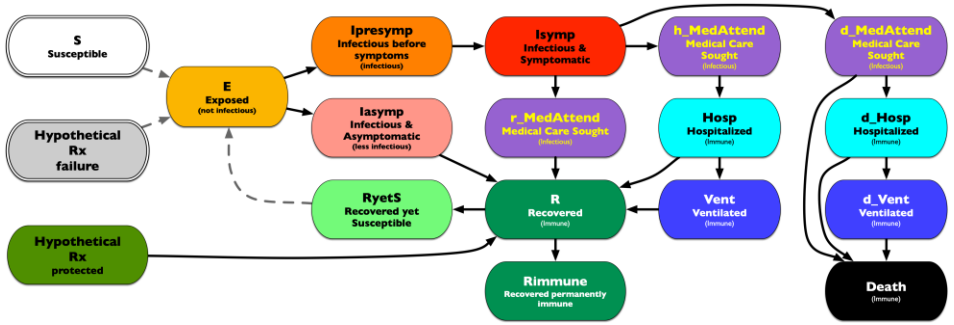
EpiHiper: Distributed network-based stochastic disease transmission simulations

- Assess the impact on transmission under different conditions
- Assess the impacts of contact tracing



Synthetic Population

- Census derived age and household structure
- Time-Use survey driven activities at appropriate locations



Detailed Disease Course of COVID-19

- Literature based probabilities of outcomes with appropriate delays
- Varying levels of infectiousness
- Hypothetical treatments for future developments